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CALCIUM AND PHOSPHORUS AND

SMITH,[1] describing the medical treatment of 314 cases of bronchial asthma writes: "When a patient was found to be sensitive, the need for general treatment was explained in detail. The general health of the subject was considered, and he was usually put on a regimen of proper rest and dietary measures, with cod liver oil and calcium lactate in moderate doses."

Novak and Hollander[2] in their study of the serum calcium of 87 patients with hay fever, hyperesthetic rhinitis and the asthmas state that the ionic calcium content of the blood serum is invariably low in hyperesthetic rhinitis and that there are also certain cases of hay fever and asthma which show a low calcium content. Calcium compounds and thyroid extract afforded temporary relief but when combined with vitamin D therapy in the form of ultra-violet irradiation it appeared to have a permanent influence on all of the rhinitis cases and upon approximately 50 per cent of those in the latter two groups.

Sterling[3] writes: "Calcium is beneficial in most hypersensitive cases whether they show a low blood calcium or not. Both calcium and phosphorus help to control the hyperexcitability of the nervous system. . . . While we cannot draw positive conclusions from a study of the above cases, calcium and phosphorus are found of great benefit in the treatment of allergic diseases. This mineral deficiency in asthmatics, hay fever, and allied diseases, whether sensitivity can be proved or not, may be the missing link which makes the allergic differ from the normal. The addition of calcium, phosphorus, and other minerals, for instance, iron, sodium and potassium salts, are possibly responsible for the favorable results in this series of cases."

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Burgess[4] is of the belief that cases of urticaria, especially those showing marked dermographism, and eczema in the vast majority of instances present a marked diminution of precipitable serum calcium. He reports that cases of urticaria and eczema were considerably improved by measures to raise the serum calcium.

Kitsuta[5] reports that in his own case he used cod liver oil and yeast for the treatment of hay fever, with beneficial results. He states: "In administering cod liver oil for the cure of hay fever already developed, I think it advisable to take about 4 teaspoonfuls three times daily. . . ."

Jones[6] found 60 per cent of his cases of exudative diathesis improved with calcium medication and parathyroid extract.

Mollison[7] states that 37 per cent of 40 cases of vasomotor rhinitis were cured and 27 per cent improved by calcium compounds and measures to increase calcium absorption.

Von Gordon[8] believes that hay fever and asthma are neuroses based upon a functional disturbance of the vegetative nervous system leading to a sympathetic hypotonia with or without vagotonia, and to a labile equilibrium of the vagus sympathetic nerves which react pathologically to normally inadequate stimuli. He contends also that a decrease in the blood calcium is one of the most important causes of this lability.

Colomb[9] states that from a therapeutic standpoint calcium is valuable for conditions associated with anaphylactic phenomena. He adds, its absorption is regulated by vitamin D.

Hutton[10] states that disturbances of calcium metabolism are likely to be present in urticaria and eczema.

Pottenger[11] thinks that calcium is definitely identified with sympathetic action. He was successful in completely relieving the paroxysms of asthma by means of calcium therapy.

Klare[12] believes that there is a relationship between the exudative diathesis of childhood and calcium deficiency. He therefore finds calcium therapy indicated in recurrent catarrh, bronchial asthma, hay fever, adenopathies and increased susceptibility to acute infections. He believes that calcium has a specific action in decreasing the hyperirritability of the autonomic nervous system.

Downing and Blumenfeld[13] report several cases of acute and chronic urticaria in which calcium therapy was effective.

Schmidt[14] found ultra-violet light of value in his own case and attributed the result partly to the antispasmodic effect of the treatment.

Ochsenius[15] points out that calcium (*Cont'd*)

1-23 Bibliography on request.

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The Journal of Allergy

VOL. IV MARCH, 1933 NO. 3

Original Articles

THE TREATMENT OF HAY FEVER WITH STANDARDIZED POLLEN EXTRACTS BASED ON THE NEW UNIT OF PROTEIN NITROGEN*

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THE last of the series of papers[1 to 5] on pollen and pollen extracts gave a method for the preparation and standardization of pollen extracts based on the protein nitrogen content of the extract. It was suggested that 0.00001 mgm. protein nitrogen (P.N.) be accepted as one pollen unit. Hence 0.0001 mgm. P.N. equaled 10 units, 0.01 mgm. P.N. equaled 1,000 units, and 0.1 mgm. P.N. was 10,000 units.

The extracts prepared in our laboratory and used last year were analyzed for both the total nitrogen and the protein nitrogen content; so that while using the old basis of total nitrogen it was possible to convert dosage in terms of total nitrogen to protein nitrogen and to standard units. In three illustrative cases cited below this has been done.

Based upon the experience of last year it is possible to formulate a schedule of unit dosage for seasonal treatment. It is believed that the presentation of these data, together with suggestions regarding the change from old to new extract in perennially treated cases, will facilitate for others the adoption of the new standard.

Seasonal Treatment.—The timothy pollen extracts prepared in February, 1932, showed a total nitrogen (T.N.) of 0.4 mgm. per c.c. and protein nitrogen (P.N.) of 0.2 mgm. per c.c., a ratio of T.N. to P.N.: 2 to 1; hence a dose of 0.001 T.N. equaled 0.0005 P.N. or 50 units. The ragweed extract of 1932 analyzed in April showed 0.62 mgm. T.N. per c.c. and P.N. 0.19 mgm. per c.c. In this case a ratio of T.N. to P.N. of 3 to 1 was used, the protein nitrogen being practically one-third the total nitro-

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gen. A dose of 0.003 mgm. T.N. of this ragweed extract equaled 0.001 mgm. P.N., or 100 units.

The dosage in terms of total nitrogen, converted to protein nitrogen and to units, is given for three cases of varying degrees of sensitivity seasonally treated in 1932.

1. Case No. 9920, aged seventeen years, had typical autumnal hay fever of four years' duration without complications. Intradermal tests with solutions of ragweed pollen extracts showed marked reaction to Solution 0.0001 mgm. T.N. (3.3 units) per c.c., obviously a very sensitive case. Treatment was successful. There were no constitutional reactions. Injections were given as follows:

CASE NO. 9920. VERY SENSITIVE

T.N. : P.N. = 3 : 1 DATE	DOSE T.N.	DOSE P.N.	UNITS
3/19/32	0.00005	0.000017	1.7
3/25/32	0.000075	0.000025	2.5
4/ 2/32	0.0001	0.000035	3.5
4/ 9/32	0.0002	0.00007	7.0
4/16/32	0.0003	0.00010	10.0
4/22/32	0.0005	0.00017	17.0
4/28/32	0.0007	0.00025	25.0
5/ 5/32	0.001	0.00035	35.0
5/12/32	0.002	0.00070	70.0
5/20/32	0.004	0.00140	140.0
5/27/32	0.007	0.0025	250.0
6/ 4/32	0.01	0.0035	350.0
6/11/32	0.015	0.005	500.0
6/18/32	0.02	0.007	700.0
6/25/32	0.03	0.01	1000.0
7/ 2/32	0.04	0.013	1300.0
7/ 9/32	0.05	0.017	1700.0
7/16/32	0.06	0.02	2000.0
7/23/32	0.08	0.027	2700.0
8/ 1/32	0.1	0.034	3400.0
8/ 8/32	0.12	0.04	4000.0
8/15/32	0.14	0.047	4700.0
8/22/32	0.16	0.053	5300.0
and 5300 units weekly to October 1st			

2. Case No. 3907, aged forty-eight years. Autumnal hay fever with asthma had been seasonally treated for the past ten years. Intradermally tested with ragweed solutions based on total nitrogen, he gave a moderate reaction to Solution 0.001 and an active marked reaction to Solution 0.01 mgm. T.N. per c.c. Under treatment in 1932 he had no hay fever, no asthma and no constitutional reactions. He always responds well to relatively low dosage. This case is one of moderate or average sensitiveness.

3. Case No. 1432, aged forty-five years. There was a history of hay fever with asthma in June and July beginning eighteen years before. She had been seasonally treated for the past twelve years with good re-

sults. In 1932, intradermally tested with timothy pollen extract, she was negative to Solution 0.001 mgm. T.N. per c.c. and gave a relatively inactive marked reaction to 0.01 mgm. T.N. per c.c., a relatively insensitive case. With treatment she had no hay fever or asthma and no constitutional reactions.

CASE NO. 3907. MODERATELY SENSITIVE

T.N. : P.N. = 3 : 1 DATE	DOSE T.N.	DOSE P.N.	UNITS
5/17/32	0.0002	0.00007	7
5/21/32	0.001	0.00035	35
5/24/32	0.002	0.0007	70
5/31/32	0.004	0.0014	140
6/ 7/32	0.007	0.0025	250
6/14/32	0.01	0.0035	350
6/21/32	0.015	0.005	500
6/29/32	0.02	0.007	700
7/ 5/32	0.03	0.01	1000
7/12/32	0.04	0.013	1300
7/19/32	0.06	0.02	2000
7/25/32	0.08	0.027	2700
8/ 2/32	0.1	0.034	3400
8/ 8/32	0.12	0.04	4000
and 4000 units weekly to October 1st			

CASE NO. 1432. RELATIVELY INSENSITIVE

T.N. : P.N. = 2 : 1 DATE	DOSE T.N.	DOSE P.N.	UNITS
3/24/32	0.0005	0.00025	25
3/29/32	0.001	0.0005	50
4/ 1/32	0.002	0.001	100
4/ 6/32	0.004	0.002	200
4/11/32	0.007	0.0035	350
4/15/32	0.01	0.005	500
4/19/32	0.015	0.0075	750
4/26/32	0.02	0.01	1000
5/ 2/32	0.03	0.015	1500
5/ 6/32	0.04	0.02	2000
5/11/32	0.06	0.03	3000
5/16/32	0.08	0.04	4000
5/20/32	0.1	0.05	5000
5/23/32	0.12	0.06	6000
5/26/32	0.14	0.07	7000
5/31/32	0.16	0.08	8000
and 8000 units weekly to October 1st			

For the titration of sensitivity by direct test we propose this year for convenience and simplicity to use solutions containing 10, 100 and 1000 units per c.c. respectively for routine work and where necessary stronger extracts of 5,000 or 10,000 units. These solutions are approximately twice as strong as those formerly used in our clinic for routine tests; hence it is not possible to present figures on classification as formerly. As a result

of our work last year, however, we can give what may be regarded as average dosage for the *very sensitive* case, that is, one marked to the intradermal test with a solution containing 10 units per c.c.; the *moderately sensitive* case (marked to 100 units); and the *relatively insensitive* (marked to 1,000 units). It is well appreciated that no set dosage is applicable to every case that is so classified. It is quite true that the early doses particularly should be given in accordance with the proposed dosage (Table I). The question essentially is with the higher dosage. Many cases will not tolerate and do not require the higher doses, while others, such as Case No. 9920 above, easily take without undue local reaction much larger doses than would be expected in one exhibiting such a degree of skin sensitivity.

TABLE I

SUGGESTED DOSAGE—SEASONAL TREATMENT—WEEKLY INJECTION

VERY SENSITIVE CASE				MODERATELY SENSITIVE CASE				RELATIVELY INSENSITIVE CASE			
DOSAGE				DOSAGE				DOSAGE			
PROT. N.	UNITS	BOTTLE	AMOUNT	PROT. N.	UNITS	BOTTLE	AMOUNT	PROT. N.	UNITS	BOTTLE	AMOUNT
MGM.			C.CM.	MGM.			C.CM.	MGM.			C.CM.
0.00005	5		0.1	0.0001	10	100	0.1	0.0005	50	500	0.1
0.0001	10	50	0.2	0.0002	20	units	0.2	0.0015	150	units	0.3
0.00015	15	units	0.3	0.0004	40	per c.c.	0.4	0.003	300	per c.c.	0.6
0.00025	25	per c.c.	0.5	0.0007	70		0.7				
0.00035	35		0.7					0.005	500		0.1
				0.001	100	1000	0.1	0.0075	750	5000	0.15
0.0005	50		0.2	0.002	200	units	0.2	0.01	1000	units	0.2
0.00075	75	250	0.3	0.004	400	per c.c.	0.4	0.015	1500	per c.c.	0.3
0.00125	125	units	0.5	0.007	700		0.7	0.025	2500		0.5
0.00175	175	per c.c.	0.7					0.04	4000		0.8
0.0025	250		1.0	0.01	1000		0.1				
				0.015	1500	10000	0.15	0.06	6000		0.3
0.003	300		0.15	0.02	2000	units	0.2	0.08	8000		0.4
0.004	400	2000	0.2	0.03	3000	per c.c.	0.3	0.1	10000	20000	0.5
0.006	600	units	0.3	0.04	4000		0.4	0.12	12000	units	0.6
0.008	800	per c.c.	0.4	0.05	5000		0.5	0.14	14000	per c.c.	0.7
0.01	1000		0.5					0.16	16000		0.8
								0.18	18000		0.9
								0.2	20000		1.0

Perennial Treatment.—With this type of treatment we meet two outstanding difficulties. One is due to the fact that certain patients receiving one injection a month are unable to keep up their maximum dose, and this in spite of the fact that we know deterioration of extract is steadily taking place. Such patients must either be injected at shorter intervals or be returned to seasonal treatment. The other difficulty lies in the change that must be made each year from the old extract to the new one. The method of standardization of extracts proposed by Cooke

and Stull[5] greatly facilitates this change. Last year when the 1932 extracts were standardized, the 1931 extracts still in use for monthly injections were analyzed at the same time. With cases under perennial treatment it was then possible to know the exact amount of active substance in the 1931 extract given in the last dose; hence the new 1932 extract could be given in an equivalent dose of active substance if so desired. On account of the possibilities of constitutional reactions, considerable caution was used in the attempt to make a complete change from old extract to new. In a preliminary approach it was found that in moderately sensitive cases the complete equivalent dose could be given in three or four divided doses given twenty or thirty minutes apart; then, that a complete dose could be given in two such divided doses at thirty-minute intervals. In a few of these cases the complete equivalent dose was given in a single injection.

One of us (J. H. B.) then undertook a careful observation on thirty-nine patients under perennial treatment, six of whom received both timothy and ragweed. Thus forty-five changes from old to new extract were made. In thirty-five changes on thirty patients, four of whom were very sensitive, the complete change was made to an equivalent dose. There was one very mild constitutional reaction in a less sensitive patient who frequently had had such mild reaction (itching of the palms of the hands) with previous monthly injections. With ten changes in nine patients, five of whom were very sensitive by test, the dose was reduced from 25 per cent to 50 per cent. There were two very mild constitutional reactions, itching of palms only, and one moderately severe in a patient whose injection was made after a five weeks' interval.

Our experience with extracts standardized on a protein nitrogen basis and used for monthly injections through the year leads us to make the following recommendations for the management of perennially treated cases:

First: The analyses of Dr. Stull on saline extracts of pollen show an approximate reduction of protein nitrogen of 50 per cent at the end of one year. To compensate for this loss by deterioration the dose of extract should be slowly increased throughout the year when possible, until it is approximately twice the dose required at the height of the season.

Second: It is assumed that the old extract is restandardized at the time the new extract is prepared and analyzed so that equivalent dosage is known. In the *relatively* insensitive case without tendency to general reactions the change from old extract to new may be made completely at one time. In the *moderately sensitive* case a complete change may be made using one-half or three-quarters the required dose first and the balance at the end of thirty minutes. In the *very sensitive* case it is wise for the present to give one-half the required dose, at the end of a week three-quarters the required dose, and in a week the full dose, and thereafter the full dose monthly.

We realize that no rule will obtain for all cases and care must always be exercised in those patients with a tendency to constitutional reactions. On the whole, we believe that these suggestions are well founded and that they will be helpful.

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THE TREATMENT OF HAY FEVER BY SPECIALISTS IN THE UNITED STATES AND CANADA

Report of an Inquiry

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THE injection of pollen extracts for the prevention and relief of hay fever is a widely used therapeutic measure. Not only those interested in allergic disorders, but rhinologists, internists, general practitioners as well as lay persons, administer extracts which are easily prepared and readily purchased. Of the patients with hay fever in this country, a figure that has been estimated in the millions, there are no data concerning the number who receive pollen therapy; although clinical statistics of treated cases, published during the past fifteen years, comprise a large series. Despite this experience, there is little uniformity of opinion concerning any of the various processes involved in pollen therapy. These include the preparation of the extract, the testing of the patient, and the injection of the specific allergen. Each entails several steps, no one of which has been generally accepted as a standardized method. These procedures have depended solely upon individual choice, and consequently comparative statistics have scarcely been possible. In order to assemble data on the subject, the Journal of Allergy undertook an investigation which is the substance of this report.

A questionnaire with a self-addressed and stamped return envelope was sent to 169 members of the Association for the Study of Allergy and of the Society for the Study of Asthma and Allied Conditions. One hundred and twenty-five replies were received. Of these, 21 were blank. They came from those not engaged in active practice, from dermatologists and otolaryngologists who do not treat hay fever, from relatives of deceased members, and from those associated in practice with physicians who had already replied. The remaining 104 questionnaires received were filled out more or less completely. In many instances there were letters and marginal notes with supplementary information and comment.

The list of questions was incomplete, but was designed for the purpose of making a concise compilation rather than to secure a wealth of detail. The form appeared as follows:

My dear Dr. .....:

The Journal of Allergy is undertaking a compilation of the factors involved in the treatment of hay fever by specialists in the United States.

It is appreciated that the appended questionnaire is not complete, but it serves the purpose of this inquiry. The information revealed in such a study depends largely upon the accuracy of individual replies. Your cooperation and prompt response will be greatly appreciated.

—THE EDITORS.

Do you buy pollen extracts? .....
Do you prepare them? .....
Do you collect pollens, or buy them? .....
What solvent do you use? .....
What is your method of standardization? (grams per cubic centimeter [1:100, etc.], nitrogen content, pollen units) .....
What are the three principal pollens in your locality? .....
Do you test by scratch method? ..... Intradermal? .....
Both? .....
Do you routinely test with foods as well as with pollens? .....
In the average case (neither excessively sensitive nor excessively insensitive) what maximum dose do you achieve? .....
As a routine, do you treat (1) Preseasonally? ..... (2) Coseasonally? ..... Both? ..... (3) Perennially? .....
Approximately what percentage of general reactions have you observed with each method? .....
What have been your total estimated results, in terms of over 90 per cent relief, 70 per cent to 90 per cent relief, less than 70 per cent relief, during the past three years? (If more than one method is used, i. e., preseasonal and perennial, state results for each.)
Remarks: .....

The answers to each question will be considered separately:

1. *Do you buy pollen extracts?*

	BUY	BOTH BUY AND PREPARE	DO NOT BUY	QUESTION UNANSWERED
No. of replies	33	14	54	3

Of the 33 who buy extracts, 8 indicated that they are purchased from other allergists, and 3 named commercial concerns. The remaining 25 of this group did not qualify their answers.

2. *Do you prepare them?*

	PREPARE	BOTH PREPARE AND BUY	DO NOT PREPARE	QUESTION UNANSWERED
No. of replies	56	14	31	1

These figures essentially check with those of question (1) and indicate that of the 3 recorded there as not answering, 2 do not buy but prepare their extracts.

3. *Do you collect pollens or buy them?*

	BUY	COLLECT	BOTH BUY AND COLLECT
No. of replies	47	10	13

The 70 replies were from those recorded in question (2) who prepare their own extracts.

4. *What solvent do you use?*

	No. of replies
Coca's fluid	25
Coca's fluid and glycerine (varying proportions)	20
Glycerine and saline (varying proportions)	8
Alcohol and saline (no proportion stated)	2
Glycerine and water (no proportion stated)	2
Dextrose (varying percentage)	2
Sodium hydroxide (varying percentage)	2
Alkaline saline (not stated as Coca's fluid)	2
Stier's solution	2
Stier-Hollister fluid	1
Coca's solution with CO_2 passed through	1
Dextrose and saline (no proportions stated)	1
Dextro-cresol solution	1
Piness' solution	1
Piness' solution and glycerine (no proportion stated)	1
Clock's solution	1
Bernton's solution	1

The word "solvent" implies extracting fluid. Three used more than one extractive. Solutions and fluids named after men who formulated them are listed as such inasmuch as they were stated in that form, rather than according to chemical constituents. There are consequently reduplications in the table.

5. *What is your method of standardization? (Grams per cubic centimeter [1:100, etc.], nitrogen content, pollen units.)*

	GM. PER C.C.	N. CONT.	POL. U.	PROTEIN UNITS	BOTH GM. PER C.C. AND N. CONT.	BOTH GM. PER C.C. AND POL. U.	QUESTION NOT ANSWERED
No. of replies	50	20	5	1	2	1	21

The term "protein units" was not explained. Of the 83 answers, 70 came from those who prepare their extracts and 13 from those who buy them. Of the latter, 10 used extracts standardized as gm. per c.c., and 3 employed material made according to nitrogen content.

6. *What are the three principal pollens in your locality?*

The purpose of this question was to determine, if possible, a correlation between the answer and the results of treatment. Apparently, hypersensitiveness to some pollens is more easily reduced than that to others. The question was justly criticized on the grounds that a predominant pollen may or may not cause hay fever. Some maintained that one or possibly two principal pollens could be easily named, but one of second or third importance was difficult to state. Others asserted that the question could not be answered at all. When the replies were tabulated, the list of pollens was so large that a correlation with the results of treatment was difficult. This was attempted and various groupings arranged, but the results were too contradictory to be considered worth recording.

7. *Do you test by the scratch method? Intradermal? Both?*

	SCRATCH	INTRADERMAL	BOTH	QUESTION UNANSWERED
No. of replies	16	27	60	1

8. *Do you routinely test with foods as well as with pollens?*

	TEST ROUTINELY	DO NOT TEST ROUTINELY	QUESTION UNANSWERED
No. of replies	56	39	9

Several stated that they test with epidermals as well as with foods. Many test on occasion but not routinely. One tests children but not adults. The answers in 3 instances were elaborated with statements that the success of treatment of hay fever is largely dependent upon a recognition of hypersensitiveness to allergens other than pollens.

9. *In the average case (neither excessively sensitive nor excessively insensitive) what maximum dose do you try to achieve?*

CONCENTRATION OF EXTRACT	MAXIMUM DOSE (IN C.C.)	NO. OF REPLIES
1:10	1.0	1
	0.5	2
	0.3	1
	0.25	1
	0.2	1
	0.05	1
1:20	0.5	3
	0.25	1
1:33	2.0	1
(3:100)	1.0	2
	0.7	1
	0.5	1
	0.3	1
	0.2	1
	0.1	1
1:50	1.0	1
	0.5	2
	0.4	1
	0.25	1
	0.1	1
1:100	1.0	6
	0.6	2
	0.5	12
	0.4	1
	0.3	5
	0.25	3
	0.2	2

MAXIMUM DOSE MG. N.	NO. OF REPLIES
0.5	1
0.3	1
0.2	1
0.15	1
0.1	13
0.05	3

MAXIMUM DOSE POLLEN UNITS	NO. OF REPLIES
200,000	1
50,000	1
20,000	1
12,000	1
10,000	1
6,000	1
4,000	1
1,000	1

Other replies were as follows: "One c.c. of the dilution giving a moderate intradermal test"; "until slight systemic or severe local reaction is noted"; "to the point of getting a negative skin test"; "the highest dose that can be tolerated"; "that reached with 50 or 60 injections."

10. *As a routine, do you treat: (1) Preseasonally? (2) Coseasonally? (3) Both? (4) Perennially?*

	PRESEASONAL TREATMENT ONLY	COSEASONAL TREATMENT ONLY	PRESEASONAL AND COSEASONAL TREATMENT	PERENNIAL TREATMENT ONLY
No. of replies	12	1	30	4

	PRESEASONAL AND PERENNIAL TREATMENT	PRESEASONAL, COSEASONAL, PERENNIAL TREATMENT	QUESTION UNANSWERED
No. of replies	11	39	7

11. *Approximately what percentage of general reactions have you observed with each method?*

PERCENTAGE OF REACTIONS	NUMBER OF REPLIES			
	PRESEASONAL METHOD	COSEASONAL METHOD	PERENNIAL METHOD	METHOD NOT SPECIFIED
0	0	1	1	6
less than 1	2	3	2	37
1	2	1	2	4
1 to 2	2	3	1	2
3 to 5	1	2	2	3
6 to 10	3	3	3	1
11 to 20	2	0	1	0
68	1	0	0	0

The question was not answered on 17 forms. Three replies stated "more with coseasonal treatment."

12. *What have been your total estimated results, in terms of over 90 per cent relief, 70 per cent to 90 per cent relief, less than 70 per cent relief, during the past three years. (If more than one method is used, i. e., preseasonal and perennial, state results for each.)*

PERCENTAGE OF RELIEF	AVERAGE RESULTS STATED IN PERCENTAGES			
	PRESEASONAL METHOD (37 REPORTS)	COSEASONAL METHOD (17 REPORTS)	PRESEASONAL AND COSEASONAL METHODS (21 REPORTS)	PERENNIAL METHOD (24 REPORTS)
90 to 100	27	38	35	49
70 to 90	55	29	56	40
Less than 70	18	33	9	11
	Method not stated (19 reports)			
90 to 100	35			
70 to 90	48			
Less than 70	17			

Thirteen did not reply to this question. Several stated that replies did not cover a three-year period. Others indicated that estimations were impressions and not accurate statistics. The percentages in each of the last 5 columns were arrived at as follows: The percentage of cases of each of the 3 groups in the first column receiving relief were added and then divided by the number of cases in the group. For instance with the preseasonal method, the percentage of the 37 patients who were estimated to have obtained over 90 per cent relief varied from none to 100. These figures were added up and then divided by 37.

COMMENT

With the exception of the last question, the replies represent a fairly accurate estimate of the methods used by those participating in this study. It is scarcely possible to record comparative results of treatment in numerical form with any degree of accuracy, inasmuch as too many variables enter into the calculations. The determination of what constitutes 90 per cent to 100 per cent or 70 per cent to 90 per cent relief in each of a large group of cases, by almost 100 observers, a matter of individual interpretation, cannot represent comparative figures. The percentage method was used, since it is the conventional one. Moreover, accurate records over a given period were admittedly not kept by all. With all methods of treatment, the range of results in each of the 3 subgroups was from zero to 100 per cent. This may be accounted for in part by the variation in pollen content of the air in different parts of the country. An attempt was made to determine whether results were generally better in the East than in the Middle West, but no conclusion could be drawn. However, since all sources of error were possible for the entire group, the averages given, if interpreted broadly, may convey a general impression.

The figures representing the results obtained by the different forms of treatment are not at variance with one another to the degree that one would expect from the great diversity in the methods of making extracts and of testing patients. One is tempted to believe, however, that comparative studies, properly conducted by a small group, would reveal the most effective way of carrying out each procedure. The results could form the basis of a standardization for the guidance of those interested in the subject and be of advantage to the great numbers of patients dependent on pollen treatment.

OBSERVATIONS ON THE FORMATION OF WHEALS. VI. RESPONSE OF NORMAL AND ALLERGIC INDIVIDUALS*

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THERE has been controversy concerning the influence of allergic manifestations upon the wheal of a positive skin reaction. Walker,[1] Pottenger,[2] Floystrup and Klagle,[3] and Rowe[4] have each maintained that positive skin reactions diminish toward the end of a severe asthmatic paroxysm and remain smaller for varying lengths of time following the attack. Under the same circumstances a complete loss of skin sensitivity wherein no reaction could be elicited has been reported by Alexander,[5] Schloss,[6] Ratner,[7] and Peshkin.[8] Freeman[9] and Hurst,[10] on the other hand, noted quite an opposite effect in that they found an increased skin response in patients during long continued asthmatic symptoms. Recently there has been much discussion concerning the question whether or not positive skin reactions diminish during the treatment of hay fever.[11]

In a previous paper, Alexander and McConnell[12] demonstrated that there is a pronounced variability in the size of wheals produced at various sites of the skin. This fact held true not only for reactions elicited in allergic individuals, but also for wheals made by histamine injections into normal subjects. As a rule, larger reactions could be obtained on the trunk than on the extremities. Injections were made at different sites simultaneously, but no information was sought concerning a possible variability in size of reactions from time to time.

The similarity of histamine wheals and those induced by allergens both in histologic structure and in the circumstances under which each is formed, has been noted by various observers.[12, 13, 14] There is a good deal of evidence which points to the fact that allergic wheals are in effect histamine wheals in that histamine or some substance akin to it seems to be released when an allergen injected into the skin comes in contact there with its specific antibody. This apparent identity permits observation of the behavior of wheals in normal individuals as well as in allergic patients both between and during attacks. The present study deals with this contrast.

METHOD

The method employed was as follows. All tests were made on the outer surface of the upper arm, care being taken that no reinjection was done at a site formerly used. Each arm was used alternately. Two one-

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hundredths of a cubic centimeter of a 1:2000 dilution of histamine acid phosphate were injected intradermally with a Luer blue barrel tuberculin syringe with a precision attachment graduated widely in 0.01 c.c. increments. The bleb raised on the skin was immediately outlined in ink, and the resulting wheal was likewise outlined at the end of fifteen minutes. Each test was made in duplicate, and unless the size of the resulting wheals approximated each other, the readings were discarded on the grounds of faulty technic. The ink markings were then copied on tracing paper and the inner and outer enclosed areas measured with a planimeter. Readings were calculated in terms of square centimeters, and the difference between the size of the initial bleb and the final reading represented the size of the wheal. The same method was followed with allergens, and the dilution on each injection remained constant. In all individuals at least eight duplicate injections were made at intervals varying from one to several days, so that it usually took three or more weeks to complete the test.

Fourteen normal and twenty-four allergic subjects each received a series of histamine injections, and those of the latter group manifesting positive skin reactions were given allergens also. In recording the results in normal subjects (Table I), the smallest wheal noted (average reading of the two duplicate injections) and the largest, are the only ones given in each case; for the purpose of this test was to show the variation in size from time to time.

TABLE I

RANGE OF VARIATION IN SIZE OF HISTAMINE WHEALS INDUCED IN NORMAL SUBJECTS OVER A PERIOD OF WEEKS

NO.	SMALLEST WHEAL SQ. CM.	LARGEST WHEAL SQ. CM.	RANGE OF VARIATION SQ. CM.
1	0.90	1.40	0.50
2	0.80	1.20	0.40
3	0.71	1.20	0.49
4	1.30	2.82	1.52
5	0.73	1.04	0.31
6	1.50	2.40	0.90
7	0.80	1.00	0.20
8	0.51	0.92	0.41
9	2.20	3.00	0.80
10	0.90	1.10	0.20
11	3.21	3.80	0.59
12	1.10	1.63	0.53
13	1.10	1.40	0.30
14	1.00	1.50	0.50

From Table I it is apparent that histamine wheals injected under controlled conditions into normal subjects show a marked variation over a period of days (Fig. 1). The average size of the smallest wheals was 1.2 sq. cm., and that of the largest 1.74 sq. cm. The average range of variation was 0.54 sq. cm. In one instance it was 1.52 sq. cm. Inasmuch as

injections were made always at one place, the inference drawn from the above experiment is that some variable constitutional factor controls the behavior of histamine wheals.

The allergic series represented ten cases of bronchial asthma, eleven of vasomotor rhinitis, and two each of urticaria, angioneurotic edema and

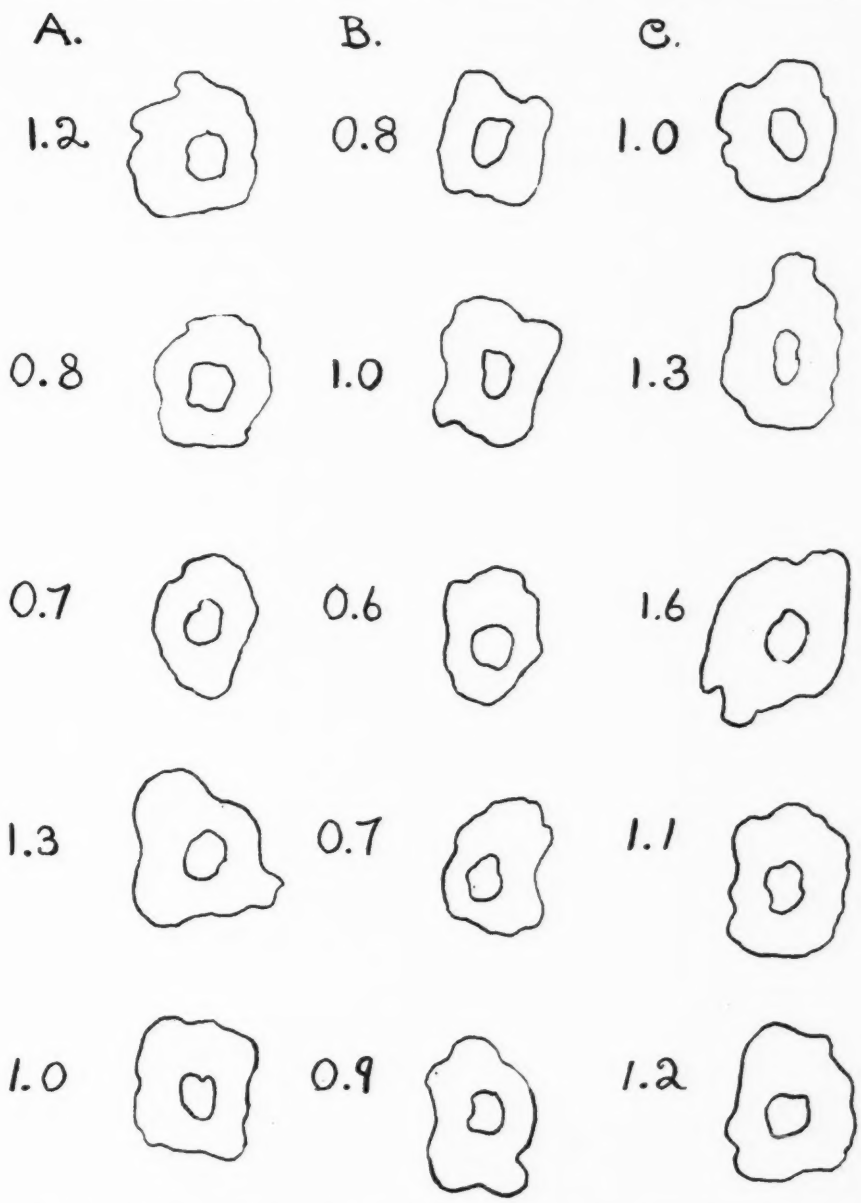

Fig. 1.—Variations of histamine wheals from day to day on three normal subjects. Wheals from 0.02 c.c. of 1:2,000 histamine acid phosphate solution injected intradermally. Figures give increase in area of wheals measured in square centimeters fifteen minutes after injection.

headache. Each was a proved case of allergy either by skin test or by history of the case with subsequent developments. The purpose of this study was to compare the behavior of histamine and allergic wheals at periods during and between symptoms. When patients were treated during attacks, care was taken to give injections when symptoms were severe and before medication. The term "between attacks" refers to freedom from all symptoms for at least twelve hours. In each case at least eight duplicate injections were made. Unlike the determinations in Table I, the measurements of all wheals were totaled and averaged during and between attacks, and thus compared (Table II).

TABLE II

A COMPARISON IN THE SIZE OF WHEALS IN ALLERGIC INDIVIDUALS DURING AND BETWEEN ATTACKS

PATIENT NUMBER	ALLERGIC MANIFESTATION	HISTAMINE WHEALS		ALLERGEN WHEALS	
		BETWEEN ATTACKS	DURING ATTACKS	BETWEEN ATTACKS	DURING ATTACKS
1	Bronchial asthma	0.91 sq. cm.	2.00 sq. cm.	0.27 sq. cm.	0.30 sq. cm.
2	Bronchial asthma	0.76 sq. cm.	1.26 sq. cm.	....	....
3	Bronchial asthma	0.80 sq. cm.	1.27 sq. cm.	....	....
4	Bronchial asthma	1.52 sq. cm.	2.15 sq. cm.	0.52 sq. cm	0.55 sq. cm.
5	Bronchial asthma	0.81 sq. cm.	1.27 sq. cm.	....	....
6	Bronchial asthma	0.93 sq. cm.	1.23 sq. cm.	....	....
7	Bronchial asthma	0.75 sq. cm.	1.02 sq. cm.	0.51 sq. cm.	0.43 sq. cm.
8	Bronchial asthma	1.10 sq. cm.	2.50 sq. cm.	2.90 sq. cm.	3.10 sq. cm.
9	Bronchial asthma	0.63 sq. cm.	1.00 sq. cm.	....	....
10	Bronchial asthma	1.00 sq. cm.	2.00 sq. cm.	....	....
11	Vasomotor rhinitis	1.05 sq. cm.	1.45 sq. cm.	0.85 sq. cm.	0.95 sq. cm.
12	Vasomotor rhinitis	0.95 sq. cm.	1.80 sq. cm.	0.35 sq. cm.	0.55 sq. cm.
13	Vasomotor rhinitis	0.70 sq. cm.	1.02 sq. cm.	0.41 sq. cm.	0.53 sq. cm.
14	Vasomotor rhinitis	0.85 sq. cm.	1.53 sq. cm.	0.28 sq. cm.	0.37 sq. cm.
15	Vasomotor rhinitis	1.10 sq. cm.	1.40 sq. cm.	2.00 sq. cm.	1.80 sq. cm.
16	Vasomotor rhinitis	0.92 sq. cm.	0.94 sq. cm.	1.60 sq. cm.	1.70 sq. cm.
17	Vasomotor rhinitis	0.80 sq. cm.	1.00 sq. cm.	0.60 sq. cm.	0.70 sq. cm.
18	Vasomotor rhinitis	0.90 sq. cm.	1.30 sq. cm.	0.50 sq. cm.	0.60 sq. cm.
19	Vasomotor rhinitis	1.20 sq. cm.	1.31 sq. cm.	1.60 sq. cm.	1.55 sq. cm.
20	Vasomotor rhinitis	1.12 sq. cm.	1.40 sq. cm.	0.95 sq. cm.	1.00 sq. cm.
21	Vasomotor rhinitis	1.10 sq. cm.	1.43 sq. cm.	1.20 sq. cm.	0.92 sq. cm.
22	Urticaria	0.95 sq. cm.	1.93 sq. cm.	....	....
23	Urticaria	0.90 sq. cm.	1.26 sq. cm.	....	....
24	Angioneurotic edema	0.75 sq. cm.	1.40 sq. cm.	....	....
25	Angioneurotic edema	1.15 sq. cm.	1.27 sq. cm.	....	....
26	Headache	1.40 sq. cm.	1.80 sq. cm.	0.30 sq. cm.	0.90 sq. cm.
27	Headache	1.30 sq. cm.	1.81 sq. cm.	0.20 sq. cm.	0.30 sq. cm.

It is noteworthy that in each instance the histamine wheals were as large and usually much larger during an attack than when the patient was symptom free. This was particularly true in the cases of bronchial asthma. The average reading of histamine wheals between attacks in the entire series was 0.977 sq. cm., and during attacks was 1.44 sq. cm. Considering that at least eight duplicate injections were made in every case, these averages each represent more than 430 readings, so that the difference is doubtless a real one and beyond the limits of error.

DISCUSSION

From these observations, the facts deduced are that in normal individuals there is a great variation in the size of histamine wheals injected at intervals. The reason for this phenomenon is unknown, and the behavior of wheal formation in normals is therefore at no time predictable. During allergic manifestations, on the other hand, one may expect a series of histamine wheals to be distinctly larger than when observed between attacks. This is particularly true of bronchial asthma and suggests that constitutional response is greater than in vasomotor rhinitis wherein the discrepancy between the size of wheals is not so great. The fact that no essential difference occurred in allergen wheals is not explained, for the reason that constitutional factors responsible for wheal formation are not known. In but one instance was an allergen wheal smaller during attacks. This seems to be in contradiction to the observations reported heretofore that in bronchial asthma wheals tend to diminish or disappear. There were, however, but four observations in the asthma series, and further confirmation is necessary before this question can be definitely answered.

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THE USE OF SUPRARENAL CORTEX EXTRACT IN THE TREATMENT OF BRONCHIAL ASTHMA*

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HARTMAN, Mac Arthur and Hartman[1] and Rogoff and Stewart,[2] working independently and at the same time, were the first investigators to isolate the cortical hormone of the suprarenal gland; but it remained for Swingle and Pfiffner,[3] in 1930, to prepare an extract which indefinitely maintained life, in normal condition, of suprarenalectomized animals. This contribution gave impetus to the clinical application of the extract in human beings suffering from Addison's disease, and many reports[4, 5, 6] of its beneficial effect have recently appeared in the literature.

The influence of the suprarenal cortex extract in conditions other than Addison's disease has been little studied. No work has been published of its use in the treatment of bronchial asthma. Patients suffering with severe and protracted asthma frequently complain of weakness, loss of appetite, loss of weight and exhaustion. The blood pressure is invariably low. There is, as a rule, a hypochlorhydria with a relatively low blood sugar. These findings are also present in Addison's disease except in a more marked degree. It seems plausible that some degree of cortical insufficiency may exist in patients with chronic asthma and that administration of the cortical hormone may prove of value in this condition.

For this investigation a study of four patients, three white and one colored, suffering with severe asthma was made. The youngest patient was twenty-two years and the oldest forty-three years. The age of onset was over twenty years in three cases and under this age in one. In three cases the onset was gradual. The duration of asthma before admission to the clinic was eighteen years in one, eight years in another, and six months in each of the other two cases. One patient was treated for more than two years before the suprarenal cortex extract was tried; the remaining three were under care for less than six months each and were selected because of the severity of the asthma.

A thorough history, a complete physical examination and roentgen-ray examination of the chest and nasal sinuses as well as electrocardiographic studies were made. A complete series of protein skin tests was performed. Three patients were found to be protein sensitive and one was non-sensitive.

Treatment with suprarenal cortex extract was begun in each case during the winter months, when asthma is usually aggravated. No other

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treatment was given while the cortical hormone was employed. Detailed records were kept of the effect of the extract on the asthmatic condition, appetite, strength, blood pressure, pulse and weight. The results of these observations are discussed under separate headings.

MATERIAL USED AND METHOD OF ADMINISTRATION EMPLOYED

The material used in this investigation was an aqueous extract* of fresh beef suprarenal cortex, prepared according to the method of Swingle and Pfiffner. Each cubic centimeter represented the hormone obtained from 30 grams of suprarenal cortex. In the present study quantitative figures of dosage are given in cubic centimeters of the extract or the equivalent amount of glandular tissue. This was found necessary for the time being because no uniform unit of dosage has been adopted.

The patients were first tested intradermally with the extract, and negative reactions were obtained. Treatment was begun with a dose of 0.5 c.c. which was gradually increased to 3.0 c.c. In one patient a maximum dose of 4.0 c.c. was given over a period of one month. Injections were given subcutaneously for the first few weeks and subsequently intramuscularly. Three to four injections were given weekly during the first month and one to two injections weekly thereafter. No soreness or redness appeared at the sites of injection, and no untoward systemic effects were encountered. The intravenous route was avoided because of the fear of general reactions.

Two patients were treated with the cortical extract for four months each; one patient for three months and one for six weeks.

EFFECT OF THE EXTRACT ON ASTHMA

Of the four patients treated with the suprarenal cortex extract, one showed marked improvement, one moderate, one slight and one no improvement. Detailed reports of the cases studied are as follows:

REPORT OF CASES

CASE 1.—P. H., colored, single, aged twenty-two years, was first seen at the allergy clinic on September 28, 1931. She gave a history of asthma of six months' duration. The onset was gradual with wheezing and cough, and subsequent attacks developed. There were at first free intervals of three to four weeks' duration; then the attacks became more

*The extract is marketed under the commercial name of Eschatin by the Parke, Davis & Company. The solution is clear, colorless and sterile. It contains minute quantities of epinephrine, less than one part in three million, but for clinical purposes the amount is considered negligible. The extract is comparatively stable, and its activity is maintained at refrigerator temperature for a long time. Since the early part of 1932 it has been assayed and standardized according to the dog unit suggested by Harrop et al. (Proc. Soc. Exper. Biol. & Med. **29**: 449, 1932). A dog unit of the extract is the minimum daily dose of cortical hormone per kilogram of body weight necessary to maintain normal physiologic conditions (appetite, body weight and the blood level of nonprotein nitrogen) in an adrenalectomized dog that has been previously held on a maintenance dose for a period of ten days. No definite standard of biologic assay of potency of the cortical extract has been uniformly accepted.

frequent and more severe especially in the two months prior to admission to the clinic. No history of any other manifestations of allergy in the patient was obtained.

Protein skin tests with the scratch method elicited only the following positive reactions; ragweed (short), one plus; elm, three plus; coconut, two plus; and squirrel and goat hair plus-minus. Intradermal tests with many food extracts were negative. A moderately positive reaction to house dust was elicited.

May 20, 1932, roentgen-ray examination of the chest revealed an increase in size and density of the hilum shadows. The nasal sinuses were roentgenographically negative. The electrocardiogram was within normal limits. The blood count and urinalysis were normal.

The patient was observed for three and a half months and during this time had about two attacks of asthma weekly. She wheezed continually, and ephedrine hydrochloride was taken for relief. A tonsillectomy was performed with no beneficial effect.

On January 9, 1932, treatment with suprarenal cortex extract was begun. She weighed 104.5 pounds (47.5 kg.), and blood pressure was 104 mm. systolic and 86 mm. diastolic.

During the first month she received eleven injections of the extract subcutaneously, beginning with 0.5 c.c. which was increased to 3.0 c.c.; the last seven doses being 3.0 c.c. each. At the end of the second week wheezing disappeared and the patient felt better. Members of her family noticed she was lively and more active. At the end of the first month she was considerably improved, and repeated physical examination of the lungs revealed no sibilant râles. Her appetite was excellent and she gained three pounds (1.3 kg.). During the second month she received eight injections of the extract subcutaneously; each dose contained 3.0 c.c. She had no attacks of asthma and wheezed only occasionally. During the third month she received only one treatment weekly, 3.0 c.c. each; the last injection being given intramuscularly. She had no attacks and felt better than at any time in the previous year. During the fourth month of treatment she also received one injection weekly, but because of an insufficient quantity of extract on hand one injection contained 1.0 c.c., another 2.0 c.c. and the remainder 3.0 c.c. each. Improvement continued. She felt as though she were "cured of asthma." The extract was discontinued on May 9, 1932. She had received twenty-seven injections containing in all 72.5 c.c. (representing 2,175 grams of suprarenal cortex).

The result in this case was considered one of marked improvement. Attacks of asthma disappeared. The patient was able to work, had little or no difficulty in breathing and wheezed only occasionally. She felt much stronger and looked decidedly improved. July 11, 1932, she was doing well, had only one mild attack and weighed 110 pounds (50.0 kg.).

Case 2.—J. P., aged twenty-six years was first seen at the clinic on November 30, 1931. He gave a history of asthma of six months' duration.

The onset was sudden. He was perfectly well until May, 1931, when his trouble began with an attack of wheezing, shortness of breath, cough and sneezing. Attacks recurred daily and required injections of epinephrine hydrochloride (1:1000). The condition became aggravated so that he had practically continuous asthma and could not work.

Physical examination revealed a robust young Italian, well developed and well nourished, dyspneic, wheezing and coughing. Sibilant and sonorous râles were heard throughout both lungs. The electrocardiogram revealed tachycardia with tendency toward right axis deviation. The blood count was normal.

Roentgen-ray examination of the chest showed moderate hilum enlargement, and the nasal sinuses were negative except for slight clouding of the antra. Protein skin tests with the scratch and intradermal methods were negative. The patient was observed for one month and was having constant asthma.

On December 28, 1931, treatment with suprarenal cortex extract was begun. The patient's blood pressure was 104 mm. systolic and 74 mm. diastolic, and his weight was 180.5 pounds (82.0 kg.).

During the first month he received thirteen injections of the extract subcutaneously, beginning with a dose of 0.5 c.c., which was gradually increased to 3.0 c.c.; the last eight injections being 3.0 c.c. each. He seemed to be improved for eight to ten hours after treatment and sometimes for one to two days. He wheezed less, his appetite was improved and he gained five pounds (2.2 kg.). During the second month he received eleven injections of 3.0 c.c. each. The first three injections were given subcutaneously and the remainder intramuscularly. The patient showed definite improvement and felt better than at any time in the previous eight months. In the third month of treatment he received eight injections of the extract intramuscularly; the first five doses contained 3.0 c.c. each and the subsequent three doses 4.0 c.c. each. He was not so well as he had been the month before. Attacks returned and were severe. During the fourth month he received ten injections; seven doses contained 4.0 c.c. each, two 3.0 c.c. each, and one only 1.0 c.c. He was generally improved and had only two or three attacks but none severe. The last injection was given on April 22, 1932. He had received forty-two injections, a total of 126.5 c.c. (representing 3,795 grams of suprarenal cortex).

The result in this case was considered one of moderate improvement. About three or four weeks after discontinuance of the extract asthma became aggravated and wheezing more constant.

Case 3.—S. P., female, unmarried, aged twenty-nine years, was first seen in the allergy clinic on November 22, 1929. She gave a history of asthma of eighteen years' duration. In childhood attacks occurred every few months and lasted a day or two. Gradually her condition grew worse, and wheezing spells became more frequent and more severe. In the six months before admission to the clinic attacks occurred practically daily

and asthma was constant. No other form of allergy was present in the patient. The family history revealed asthma in a maternal cousin and a brother.

Physical examination revealed a thin, frail, sallow, markedly underweight and undernourished female, appearing chronically ill with dyspnea and wheezing. There was moderate anteroposterior enlargement of the chest with hyperresonance on percussion. Throughout both lungs there were numerous sibilant and sonorous râles. The heart was normal and the electrocardiogram showed a right axis deviation. The blood pressure was 100 mm. systolic and 70 mm. diastolic. Her weight was 84.5 pounds (38.4 kg.).

Skin tests were performed with the scratch method, and plus-minus reactions were obtained to cat hair, dog hair, lettuce and beet. An ophthalmic test with dry pollen was negative.

April 29, 1930, roentgen-ray examination of the chest showed general parenchymatous changes in the middle thirds of both lungs. The hilum shadows were markedly increased in size and density. Roentgen-ray examination of the nasal accessory sinuses revealed the left antrum cloudly as compared to the right.

The patient received injections of nonspecific therapy and autohemotherapy in addition to various dietary regimens. Asthma was somewhat relieved, but generalized weakness became more apparent. She complained of vague pains in the arms and legs and was easily fatigued.

On February 15, 1932, treatment with suprarenal cortex extract was begun. At this time the patient was wheezing nearly constantly and complained of difficulty in breathing. Her blood pressure was 96 mm. systolic and 70 mm. diastolic, and her weight was 85 pounds (38.6 kg.).

During the first month she received ten injections of the extract, beginning with a dose of 0.5 c.c. which was gradually increased to 4.0 c.c. All injections but one were given subcutaneously; one dose of 4.0 c.c. was administered intramuscularly. During this time she showed definite improvement. There was less wheezing and less heaviness in the chest. She felt stronger and was more active. Before the use of the cortical extract she had no desire for food, but after two weeks of treatment her appetite improved markedly and she gained four pounds (1.8 kg.). During the second month ten injections of 3.0 c.c each were given; four subcutaneously and six intramuscularly. She claimed that she felt better than at any time in the previous six months or year. During the third month she received seven injections of the extract intramuscularly; four doses contained 3.0 c.c. each, one 2.0 c.c. and two doses 1.0 c.c. each. Asthma returned. The last injection was given May 9, 1932. She had received twenty-seven injections, a total of 70.5 c.c. of the extract (representing 2,115 grams of suprarenal cortex). During the following months attacks of asthma recurred but were not severe.

The result in this case was considered one of slight improvement. The

striking change noted was the increase in appetite and strength while under treatment with the cortical hormone.

CASE 4.—J. C., aged forty-three years, male, was first seen at the clinic on May 11, 1931. He gave a history of asthma of eight years' duration. Wheezing and heaviness in the chest followed a "head cold." Attacks became severe and frequent and later occurred three and four times daily. He soon learned the use of the hypodermic syringe and would inject himself with 0.5 c.c. of epinephrine hydrochloride (1:1000) five to ten times daily. He was practically in continuous asthma and had been unable to work for a few years.

Physical examination revealed a thin, pale-faced man appearing chronically ill with dyspnea and wheezing. The chest was emphysematous, and sibilant and sonorous râles were heard throughout both lungs. No abnormalities of the heart were noted. The blood pressure was 112 mm. systolic and 70 mm. diastolic.

June 23, 1931, roentgen-ray examination revealed some parenchymatous changes in both apices and an increase in size and density of the hilum shadows. Roentgen-ray examination of the nasal accessory sinuses showed small and large cells somewhat cloudy.

Protein skin tests with the scratch method elicited positive reactions with the following: timothy, three plus; June grass, and sweet vernal grass, four plus; orchard grass and plantain, one plus. Intradermal tests with a solution of ragweed short (1:50 dilution) gave a two plus reaction and ragweed giant a plus-minus.

He received pollen treatment and other forms of therapy with no apparent relief from asthma.

On November 23, 1931, treatment with suprarenal cortex extract was begun. At this time his blood pressure was 110 mm. systolic and 78 mm. diastolic, and his weight was 150 pounds (68.1 kg.).

During the first week he received six injections subcutaneously of 0.5 c.c. each of the extract. At first he seemed somewhat improved for a few hours after treatment but then attacks of asthma recurred. During the second week three injections of 1.0 c.c. each were given. Wheezing was somewhat diminished and his chest felt clearer. In the third week he received one injection of 2.0 c.c. Asthma was severe. The following week he received two injections of 3.0 c.c. each, but no signs of improvement were noted. His weight at the end of the month was 152 pounds (69.0 kg.), a gain of two pounds (0.9 kg.).

Treatment was discontinued for seven weeks and when resumed injections were given intramuscularly. Five injections were given within two weeks without beneficial effect, and the last treatment was administered on March 2, 1932.

Seventeen injections were given in all, a total dosage of 26.0 c.c. This patient received much less of the extract than any of the other three cases and when seen again on April 1, 1932, he was having severe asthma.

EFFECT OF THE EXTRACT ON OTHER SYMPTOMS

Strength.—In three of the four cases a decided increase in strength was noted. One patient felt much stronger after one month of treatment and was able to work. Another showed increased vitality and was able to walk for long distances. The generalized fatigue and vague pains in the extremities disappeared. The patient who showed no improvement in asthma exhibited no increase in strength as a result of treatment.

Appetite.—Three of the four patients showed definite increase in appetite. In one case this was very striking.

Weight.—Gain in weight was observed in three patients. During the interval of relief from asthma there was an average gain in weight of four and one-half pounds (2.0 kg.). One patient showed a gain of nine pounds (4.0 kg.) after two months' treatment. With the return of symptoms of asthma the weight curve declined. The unimproved patient showed slight increase in weight temporarily.

EFFECT OF THE EXTRACT ON BLOOD PRESSURE AND PULSE RATE

Blood pressure estimations were taken frequently during the course of treatment. Both arms were used in each case and at each sitting. No significant change in blood pressure was noted during or at the end of treatment in any case. In three patients readings were also taken twenty minutes and a half hour after injections of 2.0 c.c. and 3.0 c.c. of the extract. No immediate rise in blood pressure was noted.

The pulse rate was taken frequently in each case during the course of treatment, but no appreciable change was observed.

COMMENT

The susceptibility of the suprarenal glands to acute and chronic diseases elsewhere in the body has been emphasized in recent years.[7] Degenerative changes in the cortex with replacement by fibrous tissue and atrophy have been described. Such changes are presumed to be toxic in nature and secondary to an underlying systemic cause. In the more recent reports[8, 9, 10] on the pathology of asthma, including autopsied material of patients dying from this condition, no mention is made of the microscopic anatomy of the suprarenal glands. It seems likely that close study of these structures may reveal secondary pathologic changes in the cortex or medulla similar to those noted in other chronic diseases. Particularly in cases of severe and chronic asthma are such changes to be looked for.

That some degree of cortical insufficiency exists in patients suffering with chronic asthma was deemed probable, and based upon this assumption the suprarenal cortex extract was administered as a replacement therapy in the four cases studied in this series. It was also believed possible that the cortical hormone may stimulate the production of epinephrine in the body and thus produce a favorable influence on bronchial

asthma. According to Goldzieher[11] "destruction of one part of the suprarenal gland (cortex or medulla) will obviously involve the other, first by impairing its function and finally by producing morphological changes, such as atrophy." There is some experimental work which lends support to the view of a synergistic action between these two hormones. In the four cases of asthma included in this report suprarenal cortex extract was used to the exclusion of epinephrine in order to determine the influence of the cortical hormone on asthma and associated symptoms. Epinephrine was used only as an emergency measure, and therefore no data on the possible synergistic action of these two preparations can be submitted. At no time was any evidence obtained to suggest antagonistic action between them. In no case was an attack of asthma induced following the use of the suprarenal cortex extract, and in a total of 113 injections no untoward local or systemic reactions were encountered.

It is also possible that the cortical hormone may act on the liver and help regulate the carbohydrate metabolism. It has been suggested[12] that this is the prepotent function of the suprarenal cortex as determined by the rise in blood sugar following the use of the cortical hormone in Addison's disease. Chemical studies of the blood in cases of asthma must be carried out before any statement can be made concerning its influence on metabolism in allergy.

It is interesting to note that Perla and Marmorston-Gottesman[13] demonstrated increased resistance to infection, toxins and histamine poisoning in suprarenalectomized animals treated with cortical hormone. This suggests the possible clinical use of the extract in human beings manifesting evidence of cortical insufficiency as a result of chronic infectious diseases or in cases of allergic nature.

CONCLUSIONS

1. Four patients, ranging in age from twenty-two to forty-three years, and suffering with severe asthma (three protein-sensitive and one non-sensitive) were treated for a period of from one to twenty-seven months with little or no improvement. Suprarenal cortex extract was then used; and the effect of the hormone on asthma, strength, appetite, weight, pulse and blood pressure was carefully noted.

2. Treatment with the extract was begun with dosage of 0.5 c.c. and increased up to 4.0 c.c., the maximum dose. Injections were given three to four times weekly during the first month and once or twice weekly thereafter. Subcutaneous and intramuscular injections were administered in each case. Two patients received treatment for four months, one for three months and one for six weeks.

3. One patient showed marked improvement in asthma, one moderate, one slight and one no improvement.

4. In three of the four patients a decided increase in strength and appetite was noted, with an average gain in weight of four and one-half

pounds (2.0 kg.). The general condition of the patient was definitely improved in these three cases.

5. No appreciable change in blood pressure was noted during or at the end of the course of treatment. No influence on the pulse rate was observed.

6. The results obtained with the suprarenal cortex extract in the four cases studied and reported in this paper warrant its further trial in a larger series of cases, employing larger dosage and utilizing, if necessary, the intravenous route.

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645 WEST END AVE.

EMPHYSEMA*

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THE great majority of patients with bronchial asthma of long standing develop emphysema. Not only is this fact common clinical experience, but it has been shown in statistical studies. Before allergy was recognized, emphysema received quite as much consideration as the associated asthma. This is not the case today, although emphysema may at times be far more responsible for the attendant disability. The reasons for this discrepancy are attributed to the enormous interest which the allergic aspect of asthma has aroused, and also to the fact that there has been much confusion concerning the significance of emphysema. Cases of patients with the latter disease with large barrel chests are observed which have few if any respiratory symptoms, whereas in others the disability is great.

In the past few years an entirely new light has been thrown on the subject which has revealed not only a fairly concise classification but which also has revised time-honored beliefs concerning the heart and circulation in emphysema. Inasmuch as the subject is an important consideration to those interested in allergy, the purpose of this paper is to present a brief review.

HISTORICAL

Emphysema, as a clinical entity, was discovered by Laennec,[1] who not only described its symptoms and physical signs but demonstrated the lesion by cutting thin slices of lung wherein the distended and ruptured alveoli could be seen. Moreover, Laennec propounded a theory of etiology. He believed that the disease begins with a partial obstruction to the bronchi from mucous secretion (bronchial catarrh). Since the forces of inspiration are great, there is little difficulty in pulling air past the obstruction; but expiratory efforts are much more feeble, and difficulty is encountered in forcing the air through the narrowed bronchial lumina. Consequently, as long as obstruction persists, more and more air becomes trapped in the lungs. As a result, the alveoli distend, lose their elasticity, and finally rupture. Laennec's contribution stimulated a great interest in the disease almost immediately and led to much controversy. His theory of bronchial obstruction has been the one most seriously considered and has received clinical and experimental support. Siebeck,[2] Niessen,[3] and Jackson[4] have shown that partial obstruction to expiration leads to pronounced emphysema; and Harris and Chillingworth[5] as well as Kountz, Alexander and Dowell[6] were able to produce the condition in dogs within a week by

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inserting a ball valve into the trachea so that expiration only was impeded. These observations, together with many others, leave little doubt that obstruction to expiration promptly leads to lung distention.

Opposed to this expiratory theory is the so-called "inspiratory theory," which assumes a loss of function of a portion of the lungs from disease. The remainder of the lungs overdistend in order to compensate for the part affected. The proponents of this theory maintain that only the powerful forces of inspiration are sufficient to pull the chest out into its permanent barrel shape. There is much in favor of the contention that forced inspiration leads to the appearance of emphysema. Durig[7] and Hasselbach[8] have shown that after undue physical exertion, the chest may remain distended for days and even weeks. It is likewise known that people living at very high altitudes appear to have emphysema, and Prinzmetal[9] has shown that rats kept in an atmosphere of low barometric pressure have such a degree of lung distention that the alveoli become badly torn.

Another mechanical theory of emphysema is that dealing with deformities of the chest. Freund[10] contended that a barrel chest is due to ossification of the costal cartilages, and the lungs distend as they follow the deforming chest wall. Loeschke[11] showed that kyphosis such as occurs in Pott's disease causes so great a widening of the anteroposterior diameter of the thorax that the lungs are stretched to the point of alveolar rupture. The influence of thoracic deformities on lung distention will be considered under "senile emphysema."

In appraising the theories of emphysema, Loeschke pointed out the necessity of distinguishing between the condition of mere lung distention, such as occurs on deep inspiration, and that of actual loss of elasticity as well as rupture of lung tissue. The latter circumstance is considered essential to the definition of chronic emphysema. It is unquestionably produced by bronchial obstruction. There is much doubt whether overexertion or reduced barometric pressure within the ordinary circumstances of human life will cause lung distention of a degree sufficient to injure elasticity. At least, no report of such an effect has been found.

In contrast to the mechanical theories of emphysema are the so-called degenerative theories. Most of these were formulated soon after Rokitansky[12] (1860) described the microscopic appearance of emphysematous lungs, and are numerous. Only three need consideration. One deals with a defect in the elastic tissue of the lung. Aschoff described a case of infantile emphysema in which elastic fibers were almost entirely lacking. Familial emphysema wherein one or more children have the disease has been reported, and here, too, a lack of sufficient elastic tissue is probable. As for adults, however, reports are conflicting, but most recent work tends to refute the idea that elastic tissue is the essential fault.

A theory which has long been in prominence is based upon the observation of Isaacsohn,[13] who found the small radicles of the pulmonary vessels

which comprise the alveolar walls to be thinned out and torn. The fact that arteriosclerosis and senile emphysema are frequently associated has contributed to the popularity of this idea. The recent distinction between senile and obstructive emphysema, as well as experimental proof that the pulmonary circulation is adequate in cases of the latter type, has brought the theory of vascular degeneration into doubt.

In certain cases there is little question that infection may be the underlying cause of emphysema. Particularly is this true of the cases that follow influenzal pneumonia. Here, however, as well as in bronchitis, it appears that the infection affects the bronchi, rather than that it operates directly on the lung parenchyma.

Two main types of emphysema, therefore, are recognized. One is the obstructive form due to a narrowing of the bronchi, and the other the senile or postural form which is caused by deformities of the thoracic cage. Less frequently, other factors are probably at fault, as in familial and infantile emphysema, and in the presence of pulmonary arteriosclerosis (Ayerza's disease) wherein the lesion appears to be primarily in the vessels of the lung.

OBSTRUCTIVE EMPHYSEMA

Anatomic Changes.—The prominent pulmonary lesions of obstructive emphysema are very large lungs with rupture of many alveoli. The latter circumstance is recognized readily on inspection, by air cavities of various sizes which represent the confluence of a great number of ruptured air sacs. When occurring at the surface just beneath the pleura, they appear as blebs and bullae. Any portion of the lung may be thus affected, but the apices and mediastinal margins suffer most for they lack bony support. (Fig. 1.) In advanced cases, not only do the lungs fail to collapse because of loss of elasticity, but the pressure of trapped air may be so great that they actually protrude when the thorax is opened.

Microscopically, the typical findings are large air spaces to the inner edges of which tags of ruptured alveoli may be seen to be attached. The walls of these air cavities are very much thinned out. Inasmuch as obstructive emphysema is due to constriction of the bronchi, lesions are always found in these structures. In cases of asthma the muscle layers are much thickened. When infection has occurred, masses of cells are found in the submucosa. Here the picture is quite different, for there is infiltration of cells in the submucosa and eventually loss of elastic tissue and atrophy of the muscle layers. The weakened bronchial walls offer little resistance, and the smaller tubes, especially, are markedly dilated from the pressure of air below the closed glottis during cough. Metal casts of the bronchi reveal a great distortion from the normal aspect in that instead of a small stem surrounded by a cluster of alveoli, there is a greatly dilated bronchiole with a few distorted overdistended air sacs attached. This

great dilatation of pulmonary structures is attributed to pressure of entrapped air below the point of constriction.

Functional Pathology.—As one observes the behavior of respiration in advanced obstructive emphysema, the most striking thing is the absence of abdominal movement. The entire burden of inspiration is carried by the thorax, but since this is already distended to the inspiratory position

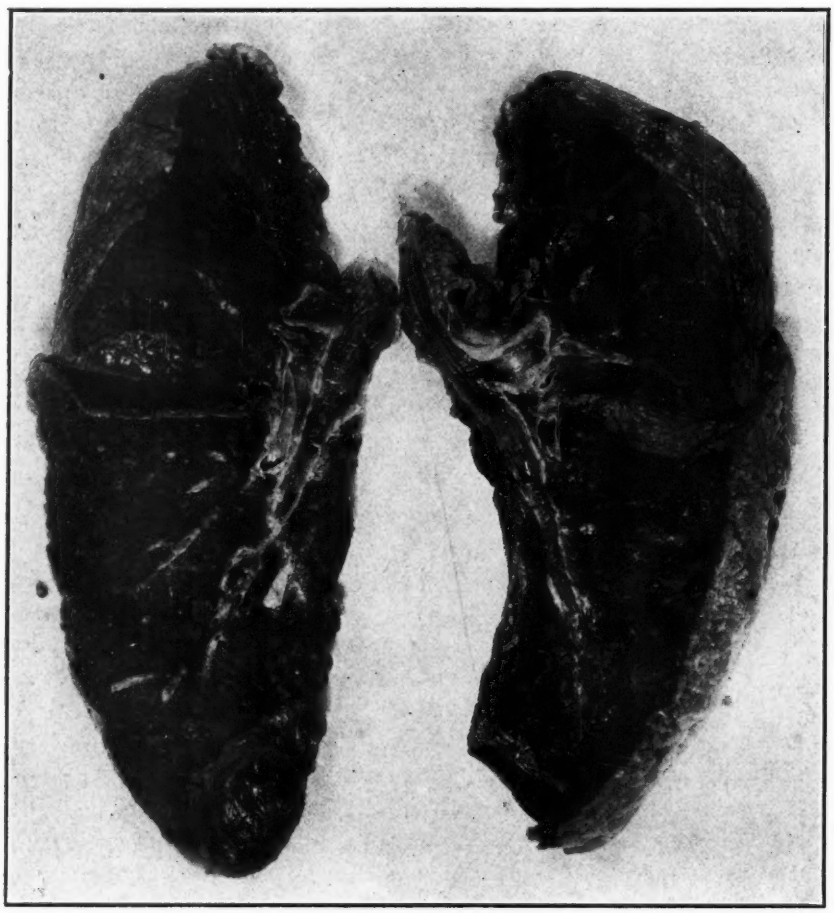

Fig. 1.—A lung from a patient with obstructive emphysema. The broad apex with air cavities is typical of the disease.

(barrel chest), at best, respiratory excursion is greatly limited. The reason for this abnormality is readily seen under the fluoroscope where a flattened diaphragm appears. The reason for this deformity is obvious, for as the lungs distend, they enlarge downward inasmuch as the resistance offered by the diaphragm is that of intraabdominal pressure which is much less than that of the surrounding bony cage.

The limitation in breathing is reflected in a reduction of the vital capacity of the lungs. In the absence of heart disease, the vital capacity is

the best estimate available of the degree of emphysema present. The height, weight, and occupation of the individual must be taken into account, but figures for normal values under these conditions have been estimated. In advanced emphysema the vital capacity may be reduced 75 per cent and more, which prohibits even mild exertion. (Table I.)

As a result of the inability to take a deep breath, the exchange of oxygen between the outer air and the pulmonary capillaries is greatly impaired, which is due to the fact that the midpoint of breathing is raised. As this occurs, the exchange of gases between the blood and outer air takes place further from the capillaries, and so the distance through which the gases must diffuse becomes increased. (Fig. 2.) Due to this faulty ventilation the oxygen content of the arterial blood becomes reduced. Even at rest,

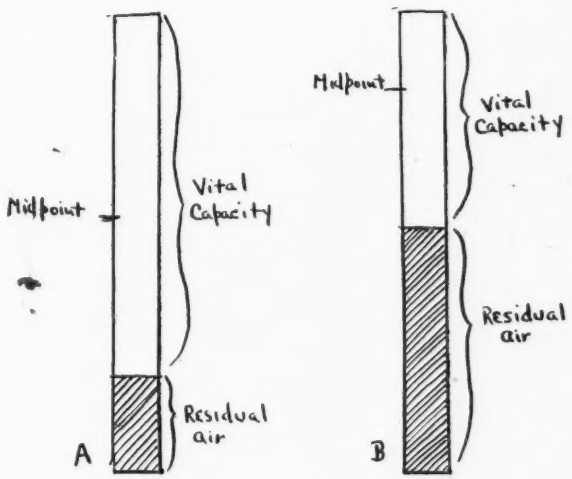

Fig. 2.—Schematic representation of relative values; *A*, normal lung; *B*, obstructive emphysema.

the oxygen saturation of the arterial blood may be less than 80 per cent, and with exercise less than 70 per cent. This defect is represented clinically by marked cyanosis.

Another result of distended lungs is an increase in intrapleural pressure. This may be so great that negative pressure disappears and values above atmospheric pressure occur. One consequence is a persistent push against the surrounding bony framework, which slowly gives until a barrel chest results. The increased intrapleural pressure is considered to have a pronounced effect on the circulation which will be discussed under that heading.

THE HEART AND CIRCULATION

Until recently, it has been believed that emphysema resulted sooner or later in heart failure. The mechanism of cardiac damage seemed quite obvious, for the pulmonary capillaries carrying blood from the right side

of the heart to the left were found to be narrowed and broken in the greatly distended lungs examined at autopsy. To drive blood through the reduced capillaries in such lungs might well throw a strain on the right ventricle, which would in time hypertrophy, dilate and eventually fail. This supposition had clinical support, for obvious signs of cardiac decompensation were found commonly in elderly individuals with the rounded barrel chests typical of senile emphysema. In younger patients, too, who had had asthma for a long time, the findings of shortness of breath on exertion as well as cyanosis, each occurring between paroxysms, seemed to indicate some trouble in the heart.

Quite recently both clinical and pathologic evidence has been presented which throws considerable doubt upon the theory that heart failure is the natural consequence of emphysema. In the past few years several investigations of the heart in cases of long standing asthma have been made. Almost invariably emphysema was present. Some of these studies were very thorough. Modern diagnostic methods were used, and critical interpretation of the findings was made. There was general agreement that in the majority of the patients examined no direct evidence of heart damage was found.

Soon after these reports were published, attention was directed to the condition of the heart as it appeared at autopsy in cases of emphysema. It then became apparent how very infrequently death from uncomplicated emphysema occurred. Until recently no deliberate examination of this question had been made. Scattered reports in the literature were confusing. Investigation proved that many cases of emphysema showed diseased hearts at autopsy, but most of these instances were in elderly people with senile emphysema. When the emphysema resulted from bronchial obstruction, the heart was usually normal.

It is now recognized that when lesions do occur, they usually appear as a generalized hypertrophy which involves both the right and the left ventricles. No adequate explanation is at hand for this phenomenon. Very rarely the right ventricle alone is enlarged, but only in cases where emphysema is associated with arteriosclerosis of the pulmonary artery.

The fact that there is little clinical or pathologic evidence of heart disease in emphysema does not appear in keeping with the older observations that the capillaries of distended lungs are narrow and broken. Recent physiologic studies have shown, however, that there is a great reserve in the pulmonary circulation. One must obliterate over one-half of the pulmonary capillary bed before there is any effect on the right heart. As a matter of fact, it has been demonstrated that as the lungs distend the capillaries straighten and fluid passes through them more readily than when they are not inflated. The observation that in patients with obstructive emphysema, dyspnea on exertion and cyanosis are common does not necessarily imply heart disease. These signs can be entirely accounted for by faulty ventilation in the lungs.

It is evident, therefore, that contrary to older theories, emphysema does not cause any material damage to the heart in the majority of cases. When lesions do occur, they are in the heart muscle and not on the valves. There is first generalized enlargement, and in time increase of cyanosis and shortness of breath on exertion appear. Dependent edema, orthopnea, râles at the bases of the lungs, and other usual signs of decompensation follow. In the earlier stages, these indications of heart damage are difficult to detect by physical signs alone. The cardiac enlargement is obscured on percussion by the hyperresonant lungs, which overlap the heart and muffle the sounds. X-ray or fluoroscopic examination of the chest, however, will readily distinguish cases in which the heart is involved. The cardiac diameters are increased in contrast to the typical elongated or spindle-shaped heart of emphysema.

In obstructive emphysema the arterial blood pressure is usually normal or below normal. On the other hand, the venous pressure is elevated and may reach a very high level. This is observed clinically by the dilated veins of the neck. Normally, the negative pressure in the thorax assists in pulling venous blood from the periphery back to the right heart. In obstructive emphysema, as the intrapleural pressure rises and actually becomes positive, flow of blood into the chest is retarded. This may have two important effects. One is that less blood enters the right heart, which instead of being overworked, as was previously believed, would actually have less blood to deliver through the lungs. Such a mechanism may have a bearing on the infrequency of cardiac decompensation. The high venous pressure as well as the cyanosis may likewise explain the dependent edema seen in some cases of emphysema without heart failure, for, according to Landis, these are the two factors most responsible for edema.

SYMPTOMS AND PHYSICAL SIGNS AND COMPLICATIONS

The outstanding symptom of obstructive emphysema is shortness of breath. In the earlier stages of the disease, this is noticeable only on exertion; but, as long as bronchial obstruction persists, dyspnea becomes progressive and more and more crippling. In advanced cases, even slow walking for any distance becomes distressing. Rarely, terminal stages are seen when great dyspnea occurs with the patient in bed. Cyanosis is extreme and eventually death occurs preceded by hours or days of unconsciousness. In the great majority of patients, however, there is a coexisting bronchitis or asthma. Paroxysmal attacks of coughing or wheezing become more and more frequent and lead to exhaustion. Under these circumstances, there is a progressive loss of appetite often accompanied by flatulence and constipation. Loss of weight, undernutrition and weakness are very common. Sleeplessness leads to irritability, nervousness, and discouragement.

Outstanding physical signs other than those in the lungs are cyanosis

and the barrel chest. The latter is variable, a fact that has been unexplained. Two individuals with emphysema, of similar age and degree of reduction in vital capacity, may show a great discrepancy in the amount of chest deformity. None whatever is occasionally observed, but only in the slender, hyposthenic type. The signs in the lungs are characteristic: increased tactile fremitus, hyperresonance to percussion with low bases, increased vesicular breath sounds, and booming voice transmission.

On fluoroscopic examination the picture is characteristic in that the intercostal spaces are widened, the pulmonary fields overilluminated, and the diaphragm is low with impaired excursion. Due to the pericardial attachment to the diaphragm, the heart is stretched in its vertical direction so that it is frequently pulled out to a spindle shape.

Bronchitis is more frequently a cause than a true complication of emphysema, but the two conditions coexist in the great majority of cases. When emphysema is produced by allergic asthma or mediastinal obstruction, bronchitis is very liable to supervene.

Pneumothorax is not uncommon and is due to rupture of an emphysematous bleb. In one case, a double pneumothorax was observed. This complication usually is not serious, since the pressure of air within the lung as well as loss of elasticity prevents complete collapse.

Hemoptysis is rare, and usually not great, although fatal cases have been reported.

Subcutaneous emphysema, or, in reality, emphysema of the deep tissues, occurs by virtue of the reflection of the pleura over the vessels of the neck and abdomen at the point where they enter the chest. The rupture of a subpleural bleb may spread air beneath the sheaths of these vessels. Under these conditions spread to the head, abdomen and legs may occur.

Treatment.—Inasmuch as obstructive emphysema, if unchecked, leads to total disability, prophylaxis is most important. Asthma and bronchitis therefore should receive early and persistent treatment. Particularly is this true in young patients before structural changes have had the opportunity to advance. Once these two conditions become chronic, not only is it more difficult to relieve them, but usually emphysematous lesions have already become established.

Under the circumstances, the cardinal principle of treatment is rest. Not only does rest tend to diminish overbreathing and therefore further overstretching of distended lungs, but pronounced improvement of bronchitis may, at times, occur. It is quite surprising how effectively bed rest may relieve symptoms of persistent cough and dyspnea. The vital capacity may show a marked elevation, and the patient be immensely relieved. Many such individuals with dyspnea, cyanosis and râles are treated for a supposed cardiac decompensation and given digitalis, but unless fluoroscopic examination should reveal a large heart, rest alone will accomplish quite as much. Ephedrine in cases of obstructive emphysema is often very

effective. Recently various mechanical measures to reduce the thoracic space have been used. Some of these may prove to be of value.

NONOBSTRUCTIVE EMPHYSEMA

In contrast to obstructive emphysema, the senile or nonobstructive type has long been recognized. This has always been assumed to be due to a

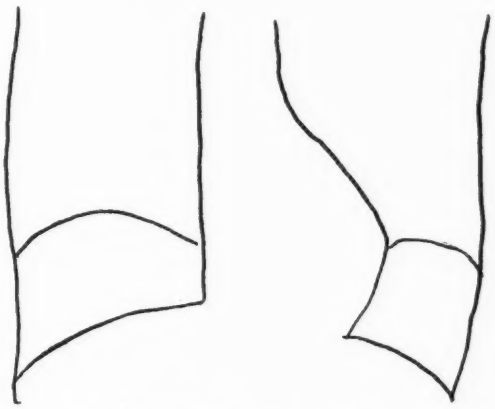

Fig. 3.—An orthodiagram of maximum respiration in a case of nonobstructive emphysema. The diaphragmatic activity is not impaired.

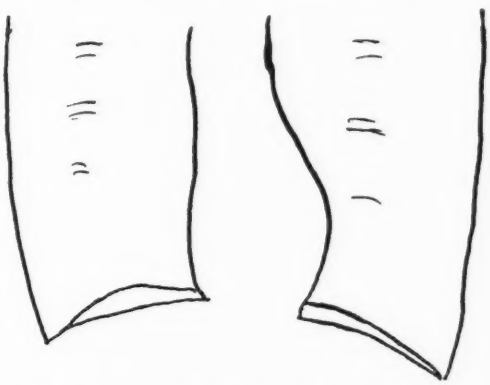

Fig. 4.—An orthodiagram of maximum respiration in a case of asthma with emphysema. There is marked reduction in diaphragmatic activity as compared to Fig. 3. These two patients were of the same general body type.

degenerative process in the lungs wherein elasticity gradually becomes lost. The frequent association of arteriosclerosis in this condition has led to the theory that changes occur in the pulmonary capillaries which make up the alveolar walls. The sclerosis of the lungs has been likened to that which occurs in the kidneys and peripheral arteries. Very little experimental work on the subject, however, has been done.

In 1932, Alexander and Kountz[14] made a comparison of respiratory function between cases of obstructive and nonobstructive emphysema. In

nonobstructive emphysema, it was noted that abdominal breathing was far more prominent than in the obstructive variety. This clinical impression was confirmed by fluoroscopic observations of the chest. The diaphragmatic excursion was greatly increased when compared to that of obstructive emphysema (Fig. 3). Moreover, in nonobstructive emphysema the diaphragmatic movements were found at times to be greater than those of normal individuals. The maximum excursion observed was 16 cm. In patients with pronounced obstructive emphysema the diaphragmatic activity was diminished at times to 1 cm. during deep inspiration (Fig. 4).

Further functional studies on each type of emphysema were compared. These included observations of the vital capacity, the oxygen and carbon dioxide content of the arterial blood, the venous and arterial blood pressures, and response to increased carbon dioxide in the inspired air as shown in Tables I and II.

TABLE I

NONOBSTRUCTIVE EMPHYSEMA

PATIENT	VITAL CAPACITY, C.C.	PER CENT OF NORMAL VITAL CAPACITY*	ARTERIAL BLOOD PRESSURE	VENOUS PRESSURE, CM. WATER	OXYGEN CONTENT ARTERIAL BLOOD, VOLUMES PER CENT	PER CENT OF SATURATION OF ARTERIAL BLOOD WITH O_2
1	3,200	89.9	160/90	5.0	18.0	96.0
2	3,400	90.8	140/85	4.5	17.4	—
3	3,800	92.0	168/78	4.5	17.2	95.0
4	3,600	85.0	205/98	6.0	18.2	94.0
5	3,300	87.4	165/87	8.2	17.6	93.0
6	2,600	75.2	175/100	5.5	18.0	94.0
7	4,000	100.0	140/87	4.0	—	—
8	3,200	87.0	175/105	4.0	—	—
9	3,700	90.0	160/90	4.4	—	—
10	3,900	96.0	127/82	5.4	18.0	94.2
11	2,700	80.0	154/98	4.8	—	—
12	2,800	85.0	120/80	5.0	—	—
13	3,300	90.0	132/82	5.5	17.8	95.0
14	3,500	85.0	210/120	5.0	—	—
15	3,600	84.0	196/105	5.5	—	—
16	3,900	92.0	187/99	5.8	18.0	95.2
17	4,000	102.0	130/87	4.8	18.1	94.3

*Based on Dreyer's tables.

The vital capacity is reduced in both types of advanced emphysema. It is, however, relatively more reduced in the obstructive than in the senile form. In the cases recorded in Tables I and II, the percentage of normal in obstructive emphysema averages 55, while in the nonobstructive type it is 85. The arterial blood pressure is usually low in obstructive emphysema but is liable to be elevated in the senile type, which usually occurs in older people, and an associated arteriosclerosis is common. The venous pressures were found to be increased in obstructive emphysema but normal in the nonobstructive form. In obstructive emphysema, the oxygen content

of the arterial blood is low, even with the patient at rest, while the carbon dioxide content may be increased. In contrast to this, the oxygen saturation of the arterial blood was recorded always as normal senile emphysema, and likewise the carbon dioxide concentration was found to be well within normal limits.

TABLE II

OBSTRUCTIVE EMPHYSEMA

PATIENT	VITAL CAPACITY, C.C.	PER CENT OF NORMAL VITAL CAPACITY*	ARTERIAL BLOOD PRESSURE	VENOUS PRESSURE, CM. WATER	OXYGEN CONTENT ARTERIAL BLOOD, VOLUMES PER CENT	PER CENT OF SATURATION OF ARTERIAL BLOOD WITH O_2
1	1,300	52.0	110/80	16.0	14.2	77.0
2	1,700	50.0	105/72	8.0	16.7	87.0
3	2,400	60.0	112/75	12.2	17.7	—
4	2,200	58.0	120/80	8.5	16.8	90.0
5	2,500	55.0	107/60	7.2	15.2	—
6	2,200	48.0	130/80	12.0	15.0	86.4
7	1,800	48.0	105/72	9.5	14.0	82.0
8	1,700	43.0	115/85	10.7	16.0	90.0
9	2,600	66.0	160/90	9.5	16.5	85.0
10	2,700	72.0	130/85	13.5	16.0	90.0

*Based on Dreyer's tables.

From these studies, it is apparent that nonobstructive emphysema leads to very little impairment in respiratory function, which throws much doubt on the supposition that the condition is primarily a disease of the lung. Some other explanation for the barrel chest and the hyperresonant percussion note in nonobstructive emphysema, therefore, was sought. It was soon noted that one constant lesion is straightness and stiffness of the thoracic spine. This is particularly true in the early stages of the disease. Although this deformity is not always obvious on an inspection of the patient, it may be readily observed on lateral views of roentgenograms of the chest and at autopsy. In contrast to this straightening, the roentgenograms of the spine of obstructive emphysema show a continuous curve.

The mechanism by which the spine assumes a more vertical position, and the influence of this deformity on the thoracic cage, were studied both clinically and pathologically. It was found that as the thoracic spine straightens the vertebral bodies separate. As the ribs are attached posteriorly to the vertebral bodies, straightening of the dorsal spine causes a separation of the ribs, and a barrel shaped chest is thus produced. It is possible to demonstrate the effect of a straight thoracic spine on the size of the chest cavity by removing all the muscles from the spine and thoracic cage of a normal cadaver and setting the base of the spine and pelvic bones in plaster of paris. When the spine is straightened so that the thoracic curve is lost, the sternum elevates and the horizontal thoracic diameters increase (Figs. 5 and 6).

The spine and bony framework of the thorax of individuals who had nonobstructive emphysema were examined at autopsy. Particular inquiry was made to determine whether the costal cartilages were prematurely ossified, and also to see whether there was fixation of the costovertebral joints. Ossification of the costal cartilages occurred in 70 per cent of cases

Fig. 5.—Chest of a normal cadaver from which all muscle has been removed. The position of the sternum is particularly noteworthy. Its upper edge stands at 15 inches on the scale.

of advanced nonobstructive emphysema but was no more frequent than in individuals of the same age group who did not have emphysema. Ankylosis of the costovertebral joints occurred in 20 per cent. If the view advanced by Freund were correct, one would expect to find ossified costal cartilages in all cases of emphysema of the nonobstructive type.

The most constant lesion found was disease of the intervertebral discs.

This was manifested as a generalized degeneration, with swelling a marked feature. The earliest change observed was swelling in the region of the nucleus, which spread outward over the annulus lamellosus. This early process could be seen in some of the discs of a given case, while in others the degeneration was more advanced and the entire disc substance swollen.

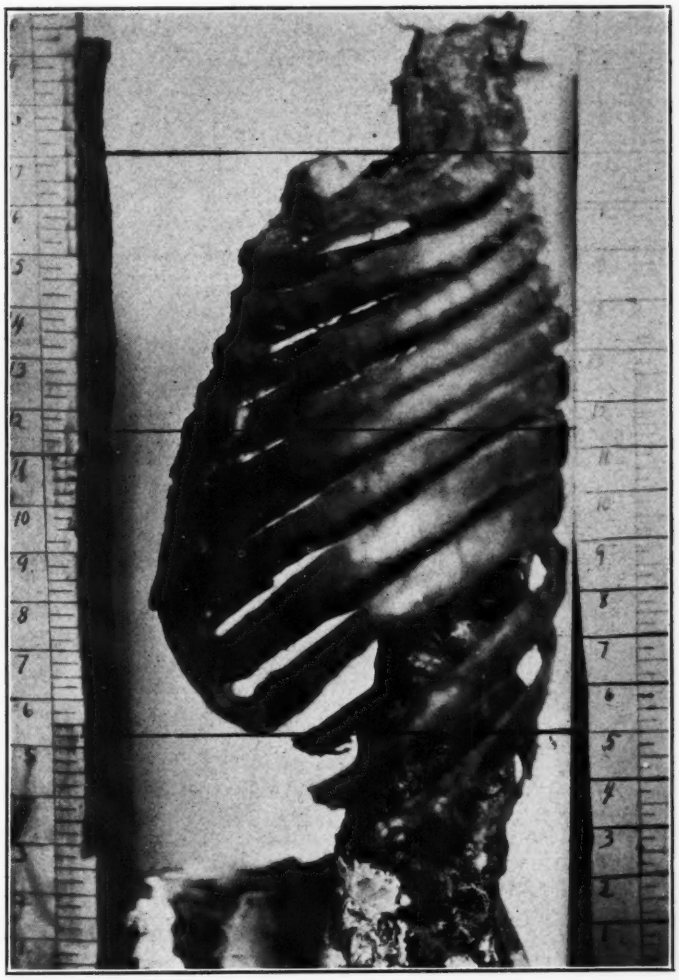

Fig. 6.—The same model as shown in Fig. 5. The thoracic spine has been straightened. The upper edge of the sternum has been raised to 17 inches. At the same time the depth of the chest from the spine to the sternum has been increased 3 cm.

On gross inspection of a disc cut across, large fissures appeared between lumps of degenerated tissue. There was usually a ring of fairly healthy annular tissue left around the edge. This corresponded to the epithelial ring.

Under the microscope, the degenerative process in the cartilage was readily seen. Large fissures were present and also areas of structureless

tissue that took an acid stain. In some discs the process had advanced to the extent that the disc became functionless and completely separated from the bone. Calcium deposits were occasionally observed in the degenerated discs, and these could be recognized in roentgenograms. Eventually, the fibers and disc substance were found to undergo complete dissolution. In writing on diseases of the intervertebral discs, Beadle[15] and Schmorl[16] have described these lesions in great detail.

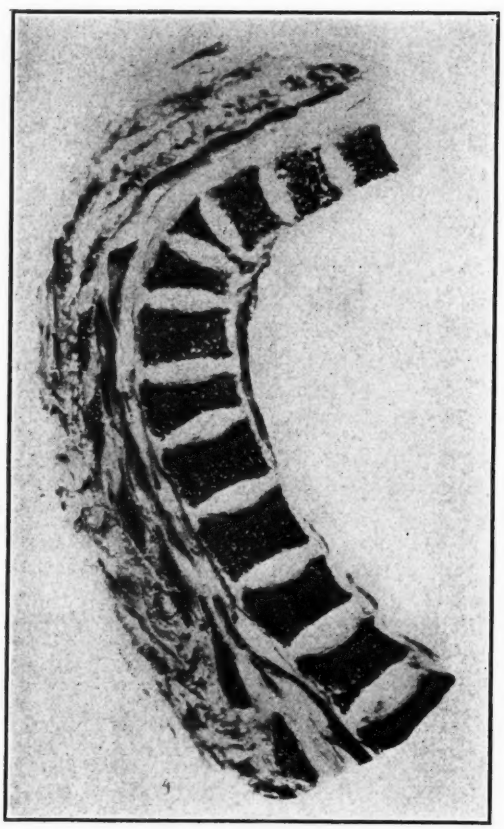

Fig. 7.—Section of the thoracic spine, showing the anatomic lesions of nonobstructive emphysema with collapse of vertebra.

As the degenerative disease of the disc progresses, the vertebral bodies become more and more invaded by the process and finally thin out. This lesion may reach the stage at which the spine can no longer support its burden, and collapse at some point then occurs. This is found in patients in whom the degenerative process is far advanced. The upper thoracic region is most commonly affected.

When the spine collapses, kyphosis results, and the marked hump in these advanced cases of senile emphysema is a familiar clinical picture. When this occurs, the upper spine sinks away from the upper end of the

sternum, which is held forward by the clavicles. The anteroposterior diameter of the chest is thus increased, and at the same time the vertical measurement of the spine is shortened. In individuals who present a kyphosis of this type, a history of loss of height may be obtained. To com-

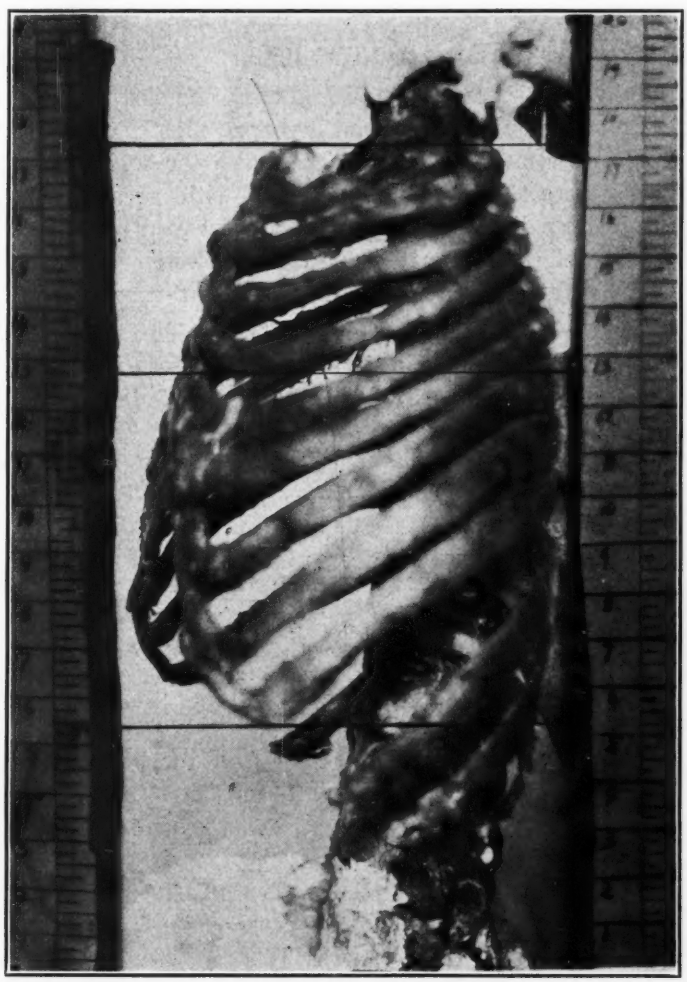

Fig. 8.—The same model as shown in Figs. 5 and 6 with the thoracic spine in an upright position. A portion of the fourth dorsal vertebra has been removed. Pressure is being directed downward and forward. The sternum is raised to above 17¼ inches on the scale. The depth of the chest at the same time has been increased 8 cm.

pensate for the shortening of the thoracic spine, the ribs flare outward and accentuate the barrel chest already present (Fig. 8).

Loeschke and others have long recognized the production of emphysema from a kyphosis of the spine. Sections of such lungs show alveolar rupture, but unless the bony deformity is very great, the lesion occurs only in the portion of pulmonary tissue that lies in the plane of the kyphosis.

Above and below, the alveoli are not involved. Lungs from patients with senile emphysema collapse when the chest is opened, and are not enlarged if the barrel chest is associated with a straight spine. When kyphosis occurs, more or less true emphysema results. Since there is little loss of respiratory function in senile emphysema, no treatment is indicated.

DISCUSSION

When emphysema is associated with allergy, the obstructive type may be assumed to be present if the patient is young. In the old chronic cases, obstructive emphysema may be associated with the senile type. Under these circumstances the thoracic deformity with great kyphosis and marked respiratory disability occurs. Not infrequently patients with a pronounced barrel chest of nonobstructive emphysema, who have some bronchitis, are referred to allergy clinics, since at first glance they resemble the chronic obstructive form. A recognition of the type of emphysema present will lead to the proper prognosis and treatment.

Those who specialize in allergy have an unusual opportunity to observe emphysema, and upon them should lie a responsibility of proper guidance for these patients.

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ANEMOPHILOUS PLANTS OF SELIGMAN, ARIZONA*

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THE problem of allergy, in so far as it concerns pollen, must be considered from the standpoint of the individual case. The average patient in the course of his daily activities seldom contacts a changing botanic environment. We have previously indicated[1] the basic problem as it applies to Santa Fe Coast Lines employees. Many of these individuals in the course of a day's work are exposed to a wide variation of altitudes, climatic conditions and, more specifically, hay fever producing plants. Such a variety of environmental conditions would practically never be duplicated in a similar distance in the East coastal or Mississippi basin states.

As we have previously indicated,[1] Needles, California, is an important Santa Fe Railroad division point and the residence of many railroad employees. The eastern termination of this division and the western termination of the Albuquerque division is Seligman, Arizona, the object of the present study. It represents a desert section 5,000 feet in elevation. Its total population, approximately 600, would by itself hardly justify a detailed botanic survey of this area, but employees from Needles, 149 miles to the west, and Winslow, 143 miles to the east, may remain in this community for eight or more hours between east and west bound trips. This is supposed to be a rest period, but botanic factors may, at certain seasons of the year, make it a period of torture instead. Thus employees living in Needles and Winslow, respectively, may experience their greatest discomfort in the Seligman section. Hence its botany may become of even more importance than that of the area in which they reside. Another purpose of this survey is to furnish a satisfactory pictorial representation of some western hay fever plants about which very little has been published.

Seligman, with an altitude of 5219 feet, is located in Aubrey Valley between the Aubrey Cliffs on the north and the mountains of the Prescott National Forest on the south. The desert plains type of vegetation found here is typical of that extending through an area of 30 to 35 miles to the east and to the west.

The climatic conditions, temperature, precipitation, etc., are typical of desert areas of a similar altitude. The charts, compiled from the most recent government reports, indicate the seasonal range of the above factors. From these charts (Figs. 1, 2, 3, and 4) it will be noted that the maximum monthly rainfall occurs in midsummer, which is also approximately the period of maximum temperatures. In marked contrast to the conditions

*From the Allergy Clinic, Santa Fe Coast Lines, Hospital Association.

reported for Needles, California,[1] this section experiences several months of winter conditions. The summer temperatures are definitely below those at Needles. The rainfall is more than twice that reported for Needles and is typically a late summer as contrasted with a spring rainy season.

The growing period, which averages approximately 155 days, is limited by the last killing frost in the spring, occurring in the latter part of April, and the first killing frost in the fall, which comes about the last week in September or the first week in October. With these facts in mind, trips

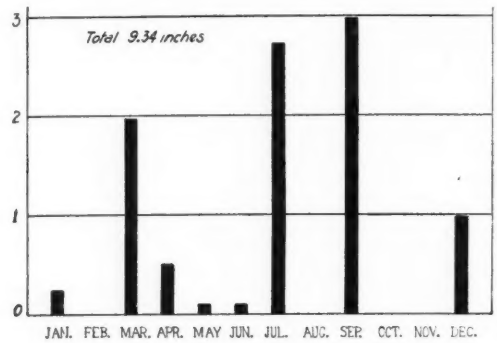

Fig. 1.—Monthly and total rainfall for Seligman, Arizona, during 1924.

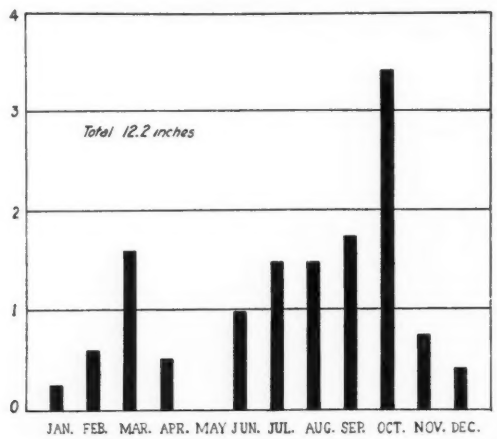

Fig. 2.—Monthly and total rainfall for Seligman, Arizona, during 1925.

were made to the area at various times during the growing season. Primary surveys were made in order to determine the best periods for intensive study. As a result, the following year two visits were made so as to include the two potentially important hay fever seasons. The first, in the latter part of May and the early part of June, was made to study the spring or "grass" season, and the second visit, in the early part of August, to include the fall or "weed" season. During the following summer another trip was made to the same area, and the previous findings were verified with a few minor exceptions due to the variation in climatic conditions.

The methods employed in making the intensive study have been previously described[1] and consist of mapping out representative sampling stations and then studying these in detail. Plants are collected and identified in the field or laboratory, and notes concerning their pollination are made. There distribution and abundance are determined by the use of belt and

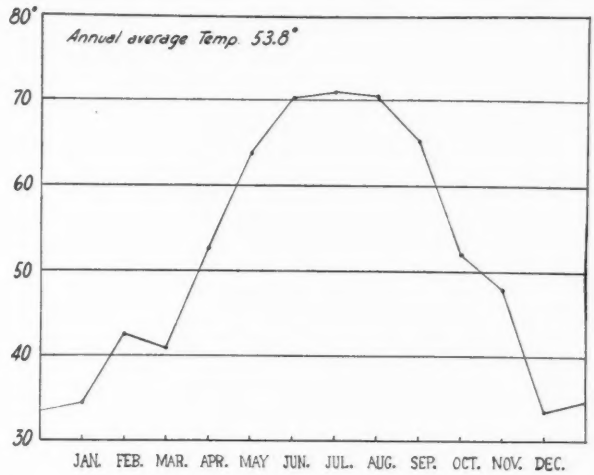

Fig. 3.—Monthly and annual average temperatures for Seligman, Arizona, during 1924.

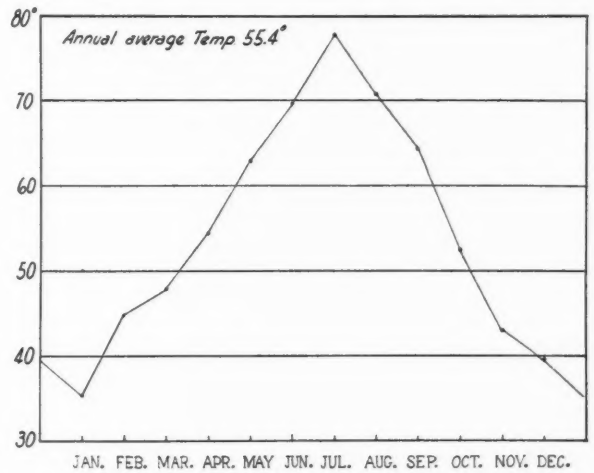

Fig. 4.—Monthly and annual average temperatures for Seligman, Arizona, during 1925.

line transects and quadrants. Photographs are taken of important individual plants and type areas.

Fig. 5 shows the location of these sampling stations and gives a general conception of the type of vegetation and the topography. In order to describe these stations better a short discussion of the important features of each will follow.

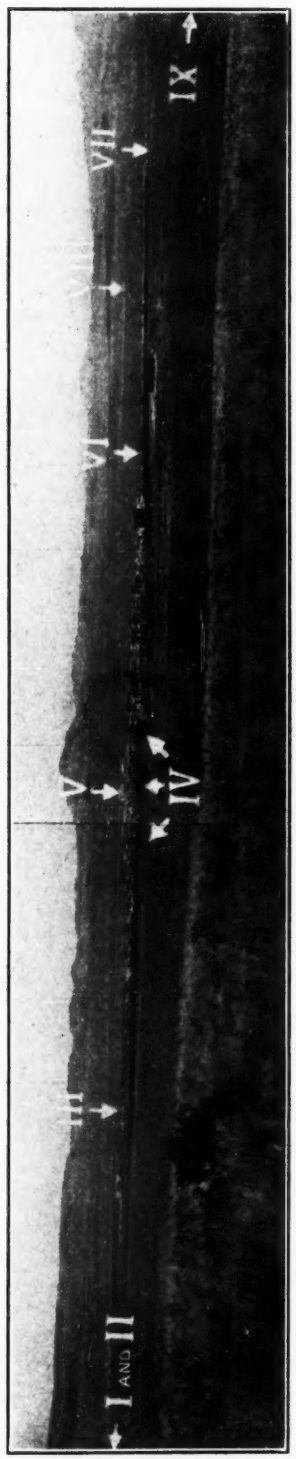

Fig. 5.—Panorama view of Seligman, Arizona, taken from a hill on the southern side of the valley. *Atriplex canescens*, a lone *Juniperus monosperma*, and remnants of the spring grasses are shown in the foreground. The whole valley floor is carpeted with *Salsola kali*.

Station I is situated about four miles west of town just north of the highway. This is the area (Fig. 6) in which *Juniperus monosperma* is found. It continues on the hills and mountains to the north. A few grasses and *Atriplex watsoni* are common, but the area is dominated by *Salsola kali.*

Station II, only one and one-half miles west of town and just south of the road, does not contain a single Juniper. *Salsola kali* is the dominant, and *Muhlenbergia porteri* and *Eurotia lanata* are the only important subdominants. This and Station I are especially important because of the prevailing westerly winds.

Station III is located on the valley floor. When first observed the area appeared to be carpeted with young very green grass, but on closer exami-

Fig. 6.—Beginning of the Junipers at Station I, showing the fields of *Salsola kali* in the foreground.

nation it proved to be a growth of rather immature and stubby *Salsola kali* (Fig. 5).

Station IV, the town area, presents a similar picture of Russian thistle dominance. A large variety of *Atriplexes* and grasses, an *Amaranth* and a *Kochia* appear as subdominants and associates.

Station V, which is directly north of town and east of the town gymnasium, is covered with the codominants *Salsola kali* and *Atriplex canescens. Chrysothamnus viscidiflorus* is also quite abundant here and is practically restricted to this location.

Station VI, just on the edge of the inhabited section of town, is composed of acres of *Atriplex canescens* (Fig. 7) in a dense practically pure stand with *Amaranthus retroflexus* near the dwellings. Had this station been omitted the importance of *Atriplex canescens* in Seligman would not have been appreciated.

Station VII, which is one-fourth mile east of town between the "National Old Trails" highway and the railroad tracks, is also dominated by *Salsola kali* with *Atriplex rosea* (Figs. 8 and 9), *Atriplex wrightii* (Fig. 10), *Chenopodium album* (Figs. 11 and 12), and two grasses as subdominants.

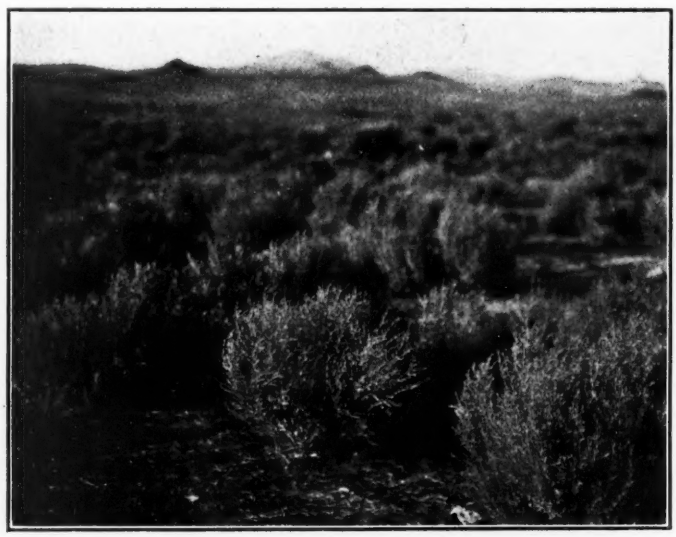

Fig. 7.—Practically pure stand of *Atriplex canescens*.

Fig. 8.—Habit of *Atriplex rosea*. In this and a subsequent picture a four-foot rule is shown.

Station VIII, also one-fourth mile east of town but north of the highway, is similarly dominated by *Salsola kali*. As one approaches the foothills, *Eurotia lanata* (Figs. 13 and 14) is seen in a patch several acres in

Fig. 9.—*Atriplex rosea* showing the detail of the leaves and fruiting bracts.

Fig. 10.—*Atriplex wrightii*, upper portion of mature fruiting branch showing the terminal staminate panicle with the two lowest branchlets bearing the pistillate bracts. Type of leaf is shown by a branch taken from the lower part of the plant.

diameter. Except for the findings at this station *Eurotia lanata* would have been considered of little or no significance.

Station IX, one-half mile east of town and a little south, is higher than

Fig. 11.—Habit of *Chenopodium album.*

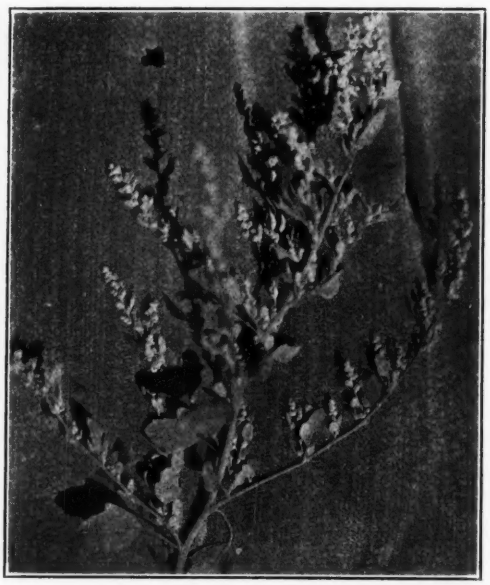

Fig. 12.—Branch of *Chenopodium album* showing leaf and flower type.

the other stations with an altitude of approximately 5260 feet. Here again the complete dominance of *Salsola kali* is unquestioned.

A composite chart of the occurrence and distribution of species at each

of the various sampling stations is shown in Table I. While this list is principally composed of the hay fever producing flora, a number of species

Fig. 13.—*Eurotia lanata*, habit view.

Fig. 14.—Branch of *Eurotia lanata* indicating type of leaf and young flowers.

which are not of the anemophilous type are included because they are so often associated with this desert type of vegetation.

TABLE I

BOTANIC SUMMARY OF SELIGMAN, ARIZONA

SCIENTIFIC NAME	COMMON NAME	STATIONS									SEASON OF POLLINATION
		I	II	III	IV	V	VI	VII	VIII	IX	
CUPRESSACEAE	CYPRESS FAMILY										
Juniperus monosperma	One-seeded juniper	**	–	–	–	–	–	–	–	–	Sp.
GRAMINEAE	GRASS FAMILY										
Aristida fendleriana	Fendler's aristida	–	**	–	–	–	–	–	–	–	Sp. Fl.
Aristida longiseta	Wiregrass	**	–	–	–	–	–	–	–	–	Sp.
Bromus tectorum	Downy brome grass	–	–	–	***	–	–	–	–	–	Sp.
Echinochloa crusgalli var. zelayensis	Mexican barnyard grass	–	–	*	**	–	–	–	–	–	Fl.
Hordeum murinum	Wall barley	–	–	–	***	–	–	–	–	**	Sp.
Muhlenbergia porteri	Mesquite grass	***	–	–	–	–	–	–	*	–	Sp. Fl.
POLYGONACEAE	BUCKWHEAT FAMILY										
Eriogonum cernuum		–	**	–	–	–	–	–	–	–	Fl.
CHENOPODIACEAE	SALTBUSH FAMILY										
Atriplex canescens	Shad-scale	*	**	**	–	***	–	–	**	–	Sp.
Atriplex rosea	Red orache	–	–	–	***	–	****	***	–	–	Fl.
Atriplex wrightii		–	–	–	***	–	–	***	–	–	Fl.
Chenopodium album	Lamb's quarters	–	–	–	–	–	–	**	–	–	Fl.
Chenopodium leptophyllum		–	**	–	–	–	–	–	–	–	Fl.
Chenopodium Watsoni		***	***	–	***	–	**	**	–	–	Fl.
Eurotia lanata	Winter fat	**	**	–	–	–	–	–	****	–	Fl.
Salsola kali	Russian thistle	****	****	****	****	***	****	****	****	****	Fl.
Kochia americana	Firebush	–	–	–	–	–	–	–	**	–	Fl.
AMARANTHACEAE	PIGWEED FAMILY										
Amaranthus retroflexus	Rough pigweed	–	–	–	***	–	–	**	–	–	Fl.
CAPPARIDACEAE	CAPER FAMILY										
Cleome serrulata	Bee plant	–	–	**	–	–	–	–	–	–	Fl.

Note.— * = Present or rare.
** = Fairly common, few.
*** = Common.
**** = Very common or abundant.
– = Does not occur.
Fl. = Pollinates in the fall.
Sp. = Pollinates in the spring.

TABLE I (CONTINUED)

SCIENTIFIC NAME	COMMON NAME	STATIONS									SEASON OF POLLINATION
		I	II	III	IV	V	VI	VII	VIII	IX	
CRUCIFERAE	MUSTARD FAMILY										
Erysimum repandum		**	–	–	–	–	–	**	–	–	Sp.
Lepidium perfoliatum	Pepper grass	*	**	–	–	–	–	–	–	–	Sp. Fl.
Lesquerella arizonica	Bladder pod	–	**	–	–	–	–	–	–	**	Sp. Fl.
Sisymbrium sophia		–	–	–	–	–	–	**	–	–	Sp.
Sophora sericea		–	**	–	–	–	–	*	–	–	Sp.
EUPHORBIACEAE	SPURGE FAMILY										
Euphorbia sps.		**	–	–	–	–	–	–	–	–	Fl.
MALVACEAE	MALLOW FAMILY										
Sphaeralcea sps.		–	**	–	–	–	–	–	**	–	Sp.
ONAGRACEAE	EVENING PRIMROSE FAMILY										
Clarkia sps.		–	*	–	**	–	–	–	–	–	Fl.
ASCLEPIADACEAE	MILKWEED FAMILY										
Asclepia mexicana	Narrow leaf milkweed	–	**	**	**	–	–	–	–	–	Fl.
LABIATAE	MINT FAMILY										
Marrubium vulgare	Common horehound	***	–	–	–	–	–	–	–	–	Fl.
SOLANACEAE	NIGHTSHADE FAMILY										
Chamaesaracha coronopsis		*	–	–	**	–	–	*	–	–	Fl.
SCROPHULARIACEAE	FIGWORT FAMILY										
Pentstamen sps.		–	***	–	–	–	–	–	–	–	Sp.
COMPOSITAE	SUNFLOWER FAMILY										
Actinella acaulis		**	–	–	–	–	–	–	–	–	Sp.
Aster leucilene		–	**	–	–	–	–	–	–	–	Sp.
Chrysothamnus viscidiflorus	Rabbit brush	–	–	–	–	****	–	–	–	–	Fl.
Circum ochrocentrum		–	*	–	–	–	–	–	–	–	Sp.
Grindelia sps.	Gum plant	–	–	–	**	–	–	–	–	–	Fl.
Gutierrezia sarothrae	Matchweed	**	***	–	–	–	–	–	–	–	Fl.
Helianthus annuus	Common sunflower	–	–	–	–	–	–	*	–	–	Fl.
Tetradymia inermis		–	**	–	–	–	–	–	–	–	Early Fl.

Summary of the Entire Area.—The hay fever problem of this community can be resolved into three potential hay fever seasons. An early spring season would be due to the pollination of the junipers. Most cases of spring hay fever would undoubtedly be caused by the group of grasses of which mesquite grass, downy brome grass, and wall barley are of the most importance and Fendler's aristida and wiregrass are of little or minor importance. The real hay fever season begins in the early summer with the pollination of the Russian thistle which reaches its height in midsummer and early fall and continues until the first killing frost around the first of October. Associated with *Salsola kali* is a large group of other *Chenopodiales.* The more important ones are *Atriplex rosea, Chenopodium Watsoni* and *Eurotia lanata. Atriplex canescens* is probably also of considerable importance because of its wide distribution, but it is not (excepting one area) found in great abundance. Of the others, *Amaranthus retroflexus* is of some importance, but *Atriplex wrightii, Chenopodium album, C. leptophyllum,* and *Kochia americana* are probably of minor importance only.

This supreme dominance of Russian thistle is in vivid contrast to the flora of Needles, California,[1] where no *Salsola kali* is to be found; yet these two towns, approximately 150 miles apart, are included under the heading of Pacific Southwest in the comprehensive list of important pollens published by certain biologic supply houses. On the other hand the two abundant *Atriplexes, Atriplex lentiformis* and *A. polycarpa,* which dominate the real pollen season in Needles are not even present in the town of Seligman. Likewise the other important *Chenopodiales* of the summer-fall season, *Atriplex canescens, A. rosea, A. wrightii, Chenopodium album, C. leptophyllum, C. Watsoni, Eurotia lanata, Kochia americana* and *Amaranthus retroflexus* are entirely lacking in the Needles area. Comparison of the other two potential hay fever seasons of Seligman with those of Needles, California, shows the same contrast and brings out with greater force the fact that the hay fever problem is a regional one! This is emphasized by Dunn[2] in her survey of the *Chenopodiaceae* in selected Southern California areas. Not only may there be a great difference between the flora of nearby towns, but the wide variation even within a small community (Table I) indicates the uselessness of trying to make "an armchair" botanic survey.

CONCLUSIONS

This survey deals with a desert section of 5,000 feet elevation. Located as it is in a valley and surrounded by foothills and mountains its vegetation is of the desert plains type with *Salsola kali, Chenopodiums* and *Atriplexes* associated. On the surrounding hills we have the *Juniperus,* and possibly also the *Pinus-Juniperus,* association. The vegetation varies greatly as one progresses from the valley floor to the foothills, and likewise many variations are noted within the basin itself.

The anemophilous plants of this area may be grouped into three potential hay fever seasons: the Juniper season, the grass season and the intense summer-fall season which is due to Russian thistle and the other *Chenopodiales* previously mentioned.

In all of our surveys we have had unlimited cooperation from the Santa Fe Hospital Association and Santa Fe Railroad. Dr. J. W. Connor has given us valuable assistance in making this survey. The photographs were made by Mr. I. F. Craig, Secretary to Mr. G. W. Simpson, Division Superintendent, Santa Fe Railroad, Needles, California.

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ATMOSPHERIC POLLEN

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A STUDY of the atmospheric pollen forms an essential part of all pollen surveys. A single season's record of the succession of species of pollens which invade the atmosphere of any given locality, furnishes by far the most valuable information regarding its hay fever potentialities. Each year the cycle faithfully repeats, with only such minor variations as may be due to seasonal variations. Consequently information gained in this way is of much more direct application to the handling of hay fever patients than even the most exhaustive botanical studies. Every community, therefore, should have its seasonal atmospheric pollen accurately determined, and recorded in a readily available form.

The accompanying chart is a record of the atmospheric pollen for the city of Yonkers, N. Y., during the summer of 1932. This record is essentially the same as those of 1930 and 1931, except that the pollen of the early flowering trees reached their maxima a little earlier in 1931 than in 1932. For example the deluge of oak pollen, always a conspicuous feature in these charts, took place on May 11 and 12 in 1931, instead of May 16 and 17 which is the time it occurred in 1932, also it was a little heavier in the latter year. As a rule, however, it is only among the early flowering trees that even such deviations as this in the time of pollination occur.

The pollen was caught from the air by exposing microscope slides coated with glycerin jelly. This material was used in preference to oil or vaseline, which are sometimes used for this purpose, because it has proved to be a much more satisfactory medium in which to observe the minute details of the structures of pollen grains, which is essential in making accurate identifications. The jelly used was prepared according to Brandt's formula,[1] with sufficient methyl green added to turn it as dark as green ink. A drop of the melted jelly was placed on the slide and spread out to cover a circular area 7/8 in. in diameter. The slide was then exposed in a horizontal position for about twenty-four hours. During the exposure it was kept under a simple cover, raised about four inches above it, to protect it from rain and direct sunlight.

After exposure the slide was brought into the laboratory, and pieces of sand, soot, etc., if present, were removed under a hand lens, the slide was gently heated to dispel any excess moisture which the glycerin is likely to absorb from the air, particularly on damp days, and covered with a No. 0 cover glass. Counting was done at a magnification of 150× (using a 10× apochromatic objective and 15× paired oculars), traversing the slide back and forth the width of the cover glass, by means of a mechanical stage.

Whenever grains were encountered whose identity could not be determined with certainty at the low magnification, the low objective was replaced by a 40× apochromatic objective with correction collar, or, if still higher magnification was needed, with a 60× apochromatic oil immersion objective (with numerical aperture 1.4), which is a lens with the highest possible resolving power and with a magnification which, though low, is sufficient to reveal all the details of the structure of pollen grains. All classes of oil immersion objectives were tried for this purpose and this was found to be greatly superior to any. Used with 15× oculars it gives a magnification of 900× which, though not the highest possible, is sufficient, and it gives greater depth of focus than those with higher magnifications. Frequently in making difficult determinations it became necessary to measure the grains. This was always done by means of an ocular micrometer used with a 20× ocular and a 90× objective to gain the advantage of maximum magnification.

All identifications were made by actual comparison with specimens in a reference collection, which included pollens of all the wind pollinated plants, and many others, of the region, mounted in glycerin jelly. Comparisons were always made by means of the 60× oil immersion objective, though after the grains had once been learned, it was found quite easy to recognize them with much lower magnifications, even as low as 150×, the magnification used for counting.

The building where the slides were exposed is five stories high, and stands on a slight eminence near the business center of the city. This elevation was chosen to gain general average conditions by avoiding the effect of the immediately local vegetation. It perhaps accounts for the relatively low grass count; for the grains of most kinds of grass are rather large, distinctly larger and less buoyant than those of the pollen of such plants as the ragweeds. However, this is perhaps less of a disadvantage than having the count overbalanced by the pollen from the plants of the immediate vicinity as would be the case at ground level. Even at this elevation above the ground the immediately local flora is reflected to some extent in the pollen count. For example, several large trees of both Osage-orange and mulberry are growing in the grounds of the laboratory. As a consequence the pollen counts of both of these are obviously unduly high. Throughout the rest of the region these two species are relatively rare, much less abundant than sweet gum, for example, which their pollen counts greatly outnumber on the chart.

The city of Yonkers is situated in the Hudson River valley, virtually at sea level. To the north and east, beyond the limits of the city, the country is partly built up and partly wild. The suburban sections are nicely cultivated, but the greater portion of the rest of the area is badly or not at all cultivated, and is fully invaded by a diversified weed flora. The entire region appears to have been in the past a mixed forest of oaks. Of course the majority of the trees have been destroyed, but many remain, some of

great size and age. The commonest species of the oaks which remain are black, white, chestnut, scarlet and swamp white. To the southeast and south lie the great metropolis of New York and its suburbs, covering a region of which the vegetation is for the most part reduced to a minimum. To the west lies the Hudson River, and on its opposite bank, which is the New Jersey shore, about a mile from the city, stand the Palisades, rising five hundred feet above the level of the river. Their tops are heavily wooded with a young second growth mixed forest which extends westward only a short distance to be replaced by improperly cultivated farm land, harboring many weeds and extending many miles westward. To the south of the Palisades, in a southwesterly direction from the city, lie the famous New Jersey meadows. It appears that much of the pollen caught on the slides originated in these adjacent parts of New Jersey, because the count has a tendency to rise abruptly as the wind swings into a westerly direction. And the New Jersey meadows appear to have been the only possible source of the cat-tail pollen, which is that of *Typha angustifolia*, a species which, while abundant in the New Jersey meadows, is rare on the New York side of the river.

The first grains to be caught on the slides in the springtime were those of juniper. The different species of juniper cannot be distinguished in their pollen, but *Juniperus virginiana* L. is the only one common enough in the vicinity to produce the pollen recorded. The curious fluctuations represented in the bulges of the curve of this species on April 5 and 23, and May 6 are due to weather fluctuations. This is indicated by the fact that similar fluctuations occur in the curves of one or more of elm, alder, hazel, maple, poplar and birch at the same times.

Birch pollen is represented throughout the month of May, extending even a little into June. There are three species of birch common in the vicinity of Yonkers, white, black and yellow. Their pollens can be distinguished from each other only upon careful and minute examination of each grain, a task which is scarcely feasible in making pollen counts. The different species of birch pollinate in the succession named, generally with considerable overlapping. The first two bulges in the birch graph represent the flowering of the white birch (*Betula populifolia* Marsh.). The third bulge, with its minor fluctuations which are due to weather variations, represents the flowering of the black birch (*Betula lenta* L.) and the fourth represents the yellow birch (*Betula lutea* Michx.).

Oak pollen began to be caught about the first of May and reached a count of about 20 grains on the second. Thereafter only occasional grains were caught until May 16 and 17 when the count suddenly increased to 1034 and 1308 respectively; after which it dropped off considerably, but rose again on May 23 to 644. These two major bulges in the graph repeat themselves from year to year and are undoubtedly due to different groups of species. At the time of the oak pollen maxima the atmosphere is actually hazy with oak pollen. Nevertheless, in spite of its great abundance, which

outnumbers all other species, oak pollen rarely causes any hay fever in the region.

In recording the pollen counts of the different grasses no attempt was made to distinguish the grains of the different species by their microscopic characters. But the different species can be separated out to some extent in the graph by taking into account their times of flowering. The first grains of grass appear toward the end of April, when the only species flowering was low spear grass (*Poa annua* L.). The count thereafter soon increased, reaching about 20 on May 8, as sweet vernal grass (*Anthoxanthum odoratum* L.) came into bloom. Toward the end of May, June grass (*Poa pratensis* L.), quickly followed by orchard grass (*Dactylis glomerata* L.), began to flower. The maximum of their flowering is represented by the double pointed bulge in the grass pollen graph of June 4 and 7, when the counts reached about 140 grains. As those two species completed their flowering, the grass pollen count fell off rapidly and continued low until the flowering period of timothy (*Phleum pratense* L.) which began about the end of June. This was soon followed by red top (*Agrostis palustris* Huds.) and the bent grasses (*Agrostis tenuis* Sibth., etc.) whose maximum flowering period is reflected in the bulge of the grass pollen graph occurring between July 11 and 15. This graph shows that timothy, in spite of the great emphasis that has been laid upon it in most hay fever literature, stands no better than third in the list of grasses for Yonkers; its pollen production is considerably less than that of June grass, orchard grass and red top. After the cessation of flowering of red top and the bent grasses, with which early summer hay fever in Yonkers virtually ends, the grass count continued low, with a minor unexplained increase on August 9, until the beginning of September when crab grass (*Syntherisma sanguinalis* [L.] Dulac) and goose grass (*Dactyloctinium aegyptium* [L.] Richter) came into flower causing the grass count to show a noticeable increase which reached a maximum on September 6. After this final flare-up in the grass count, grass pollen continued to be caught, only two or three grains at a time, until the end of the season.

The first grain of ragweed, which proved upon examination to be of the giant ragweed (*Ambrosia trifida* L.), was caught on August 8, only a few days after the first plants of that species were observed in flower. For about the first week thereafter the ragweed pollen caught proved to be entirely or predominantly of the giant species. But as the count increased, pollen of the dwarf species (*A. elatior* L.) was added, and throughout the greater part of the season the pollen of the two species appeared to be represented by about equal numbers of grains. The combined ragweed count gained rather steadily, reaching its maximum on August 29. The diminution shown in the graph between August 22 and 27 was due to unfavorable weather conditions which were likewise reflected in the graphs of all other species recorded during that time. The sudden diminution occurring in the ragweed count on September 1 is unexplained. It is apparently not

due to unfavorable weather conditions, since it is accompanied by an increase in the pollen count of the other species. With other minor fluctuations the pollen of the ragweeds continued with dwindling count until well into October. In the Yonkers region the late summer hay fever, which is due almost entirely to the two ragweeds, starts between August 15 and 20 and usually stops toward the end of September or early in October, and throughout the season its severity runs closely parallel with the pollen count of the two ragweeds.

Pine: It is not possible to distinguish the different species by their pollen. Undoubtedly several are represented in the graph. The bulk of the pollen caught toward the end of May and the beginning of June corresponds to the flowering period of *Pinus nigra* var. *austriaca* Asch. and Grab. which is extensively cultivated in and around Yonkers.

Hemlock (*Tsuga canadensis* [L.] Cass.): Trees are scarce within the city limits but are fairly abundant outside.

Spruce: Species unknown, but its pollen graph, extending over only three days, corresponds to the flowering of *Picea rubens* Sarg.

Sedge: The different species are not easily distinguished in their pollen, but the first few grains caught in April and May correspond, in point of time, to the flowering period of *Carex pennsylvanica* Lam, while those caught later in May correspond to *C. stricta* Lam.

Willow: The first grains caught correspond, in point of time, to the flowering period of *Salix discolor* Muhl. and the latter to *S. fragilis* L.

Elm: *Ulmus americana* L. is exceedingly abundant throughout the region. Several other species also occur sparingly, but no attempt was made to distinguish their pollen from each other. A single grain of elm pollen was caught on the slide late in September. This may have been from a tree of *Ulmus serotina* Sarg., a late flowering species native of the south but occasionally planted northward.

Alder (*Alnus incana* Moench.) is abundant throughout the region.

Hazel: Both the native species *Corylus americana* Walt. and *C. rostrata* Ait., and the European species *C. Avellana* L. occur sporadically throughout the region, but their pollen grains are not distinguishable from each other.

Maple: The pollen grains of the different species are not distinguishable from each other; but the first occurrence of maple pollen on the slides corresponded to the flowering of silver maple (*Acer saccharinum* L.) which is much planted in and about the city, and flowers ahead of all the others. It is followed by red maple (*A. rubrum* L.), sugar maple (*A. saccharum* Marsh.), Sycamore maple (*A. Pseudo-platanus* L.) and Norway maple, (*A. platanoides* L.) which probably all contributed to the maple pollen count recorded in the graph.

Poplar: The species of poplar were not determined. *Populus Eugenei* S.-L. is the most abundant species within the city limits, but, being an

artificially produced hybrid, it sheds but little pollen, and this mostly abortive, consisting of misshapen grains and empty skins. A part of the pollen caught answered this description. Beyond the limits of the city *P. deltoides* Marsh. and *P. grandidentata* Michx. are abundant, and it is probably from them that most of the poplar pollen was derived.

Sycamore (*Platanus occidentalis* L.): Is common throughout the region, two trees of this species grow within the laboratory grounds.

Ash (*Fraxinus americana* L.): Is abundant throughout the region.

Beech: The different species of beech pollen were not distinguished, but the long period over which beech pollen was caught suggests that more than one species was involved. Both the native species, *Fagus grandifolia* Ehrh., and the introduced European species, *F. sylvatica* L., in several varieties, are abundant.

Sweet gum (*Liquidambar Styraciflua* L.) is exceedingly abundant throughout the region.

Walnut: Both the black walnut (*Juglans nigra* L.) and the butternut (*Juglans cinerea* L.) are found sparingly throughout the region. Their grains can be distinguished from each other, but were not separated in making the counts, though both occurred.

Hickory: The pollen grains of the local species of hickory cannot be readily distinguished from each other. *Carya ovata* (Mill) Koch., *C. alba* (L.) Koch, *C. glabra* (Mill.) Spach. and *C. cordiformis* (Wang.) Koch. are found in the region.

Tree of heaven (*Ailanthus glandulosa* Desf.), an Asiatic introduction, is abundant in the region.

Plantain: The species recorded in the graph is entirely English plantain (*Plantago lanceolata* L.). Grains of the other two species (*Plantago major* L. and *Plantago Rugelii* Dene.) which grow commonly in the region, were only occasionally caught on the slides, a grain or two at a time. The pollens of these three species are easily distinguished from each other.

Chenopod: Under this name are included the pollen of lamb's-quarters (*Chenopodium album* L.), Mexican tea (*C. ambrosioides* L.), and the pigweeds (*Amaranthus retroflexus* L., and *A. hybridus* L.). All four are common and their pollen cannot be separated with certainty.

Artemisia (*Artemisia Absinthium* L.) is a recent introduction, adventive from Europe.

Goldenrod: The different species of goldenrod cannot be distinguished in their pollen. Many species occur in the region, some of them in great abundance, but one species *Solidago speciosa* Nutt. greatly outranks all others in its production of pollen.

Sunflower: The fact that sunflower (*Helianthus annuus* L.) is cultivated in considerable quantities in the grounds of the laboratory probably explains the presence of sunflower pollen on the slides.

Fleabane: *Erigeron canadensis* L. and *E. strigosus* Muhl. are exceed-

ingly common. Their pollen grains, however, are not distinguishable from each other.

Hop (*Humulus Lupulus* L.) occurs sporadically.

Linden (*Tilia americana* L.) occurs in several varieties.

Besides the pollen species which are shown in the graph, a few grains of rush, wild cherry, privet and sumac, and the spores of horsetail, several ferns and many fungi, including *Alternaria*, were caught.

After a hay fever patient has been properly typed, a glance at a chart of this kind will tell him whether or not, or just when he is likely to have hay fever in the locality for which the chart has been prepared. It is therefore imperative that every locality, particularly those that cater to the tourist traffic, and hay fever resorts in particular, should have such charts available for the inspection of prospective visitors who may be hay fever sufferers, or for physicians who wish to learn the most favorable places to which to direct their patients. It is for this purpose that the accompanying chart is presented.

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A STANDARD FOR READING SKIN TESTS*

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VARIOUS designations are in use at the present time for the reading of the degree of reactivity of the skin test when done by the intracutaneous technic, particularly in the allergic field and in some of the infectious diseases. The commonest, probably, is the grading from 1 plus to 4 plus, according to the size of the wheal, number of pseudopods, and extent of erythema, there being no agreement as to the definite size of the reaction for a particular reading often even among workers in the same clinic. Some use the "slight, moderate, marked, very marked" scale for interpretation, while others encumber their records with figures actually measuring the size of the wheal, the erythema, and the pseudopods. Of course, a photograph or tracing of the tested site would be the ideal way of recording it, but, needless to say, this is not often possible.

It seemed desirable to devise, therefore, a simple method for the reading of the skin test and by its adoption generally to encourage uniformity in the procedure. The following is suggested, as a simple and practical scale, to workers in the particular fields; although its use may be extended elsewhere.

A sheet of "absolite" or "plastocele" (a modified celluloid) 9 by 16 cm. is ruled off in 1 cm. squares. Four eye holes are made of the following diameters: 1, 1.5, 2, 3 cm.

When the fested site is ready to be read, the scale is placed so that the center of the hole closest approaching the size of the wheal is over its approximate center. If we call the four holes 1, 2, 3 and 4 plus in the order of size, the reading of the particular test would correspond to the hole which it most closely approximates in size. At the same time the surrounding erythema may be measured off in centimeters or fractions thereof, vertically and horizontally. While it is true that very irregular wheals with numerous pseudopods cannot be read by any circular standard, a close enough estimate can be made and the special character noted. (Fig. 1.)

For the purpose of standardization it should be emphasized that the original wheal created by the injection should be 0.5 cm. in diameter (specimen size is shown on the scale). For those who may wish to use a smaller scale the following diameters are suggested: 0.75, 1.25, 1.75 and 2.5 cm., and the holes may be placed in order alongside the larger ones.

*From the Allergy Clinic, New York Hospital.

The scale may then be called the A (larger) and B (smaller). The general adoption, however, of one or the other would be desirable, and it would seem that for all purposes the larger scale is preferable. (Fig. 2.)

The need for uniformity in the interpretation of the intracutaneous

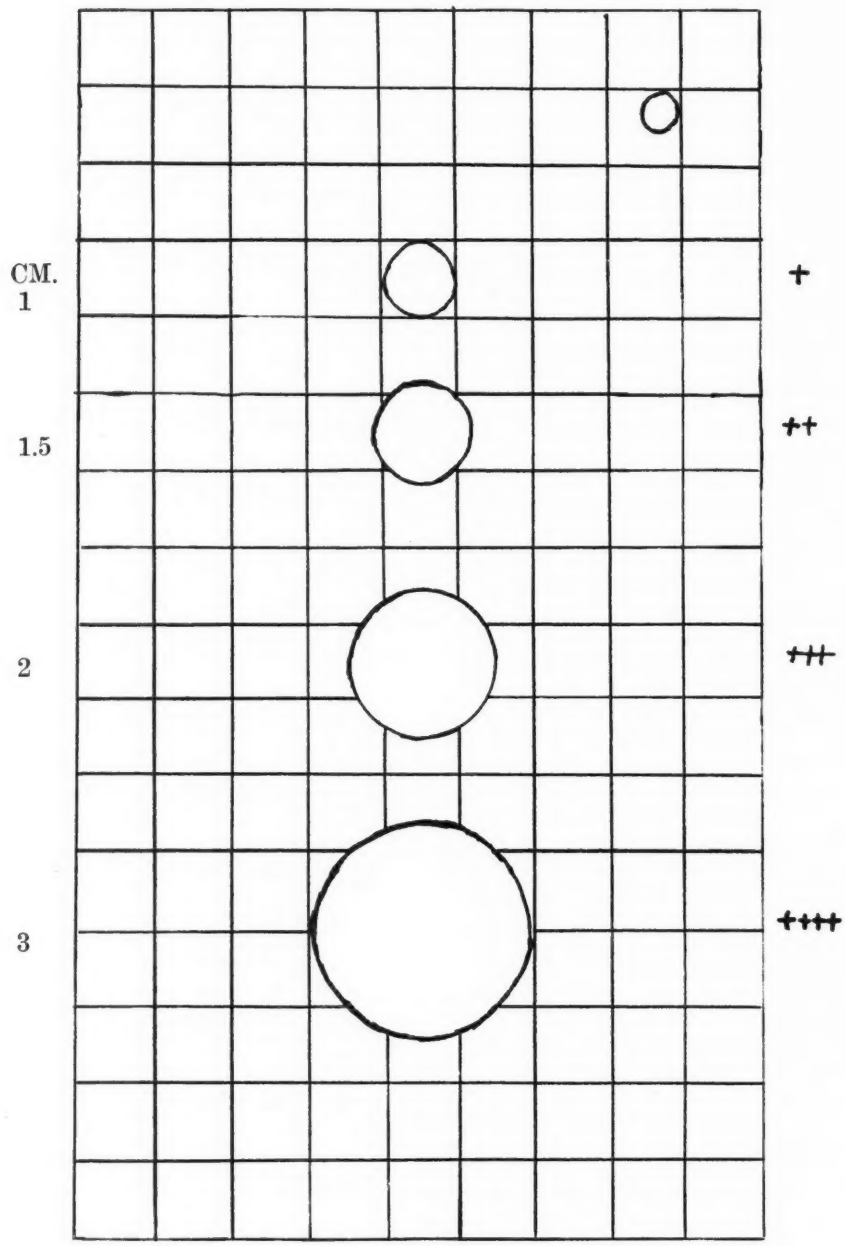

Fig. 1.

tests is the prime reason for the proposal of this scale, its practical simplicity being an added feature.

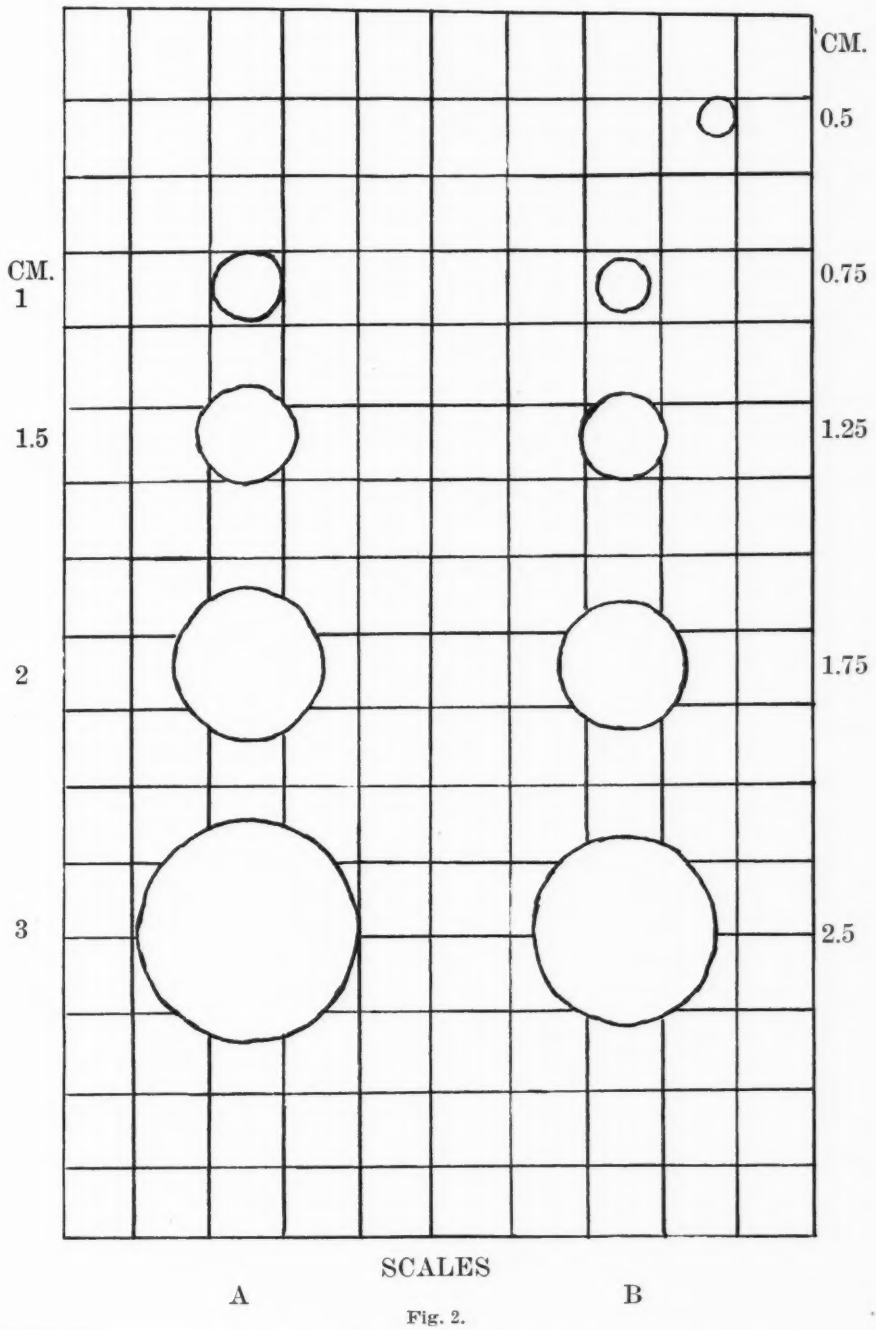

Fig. 2.

The "Cutometer" is obtainable from G. Tiemann & Co., 107 E. 28th Street, New York City.

Department of Reviews and Abstracts

Selected Abstracts

The Pollen of the Fave Bean (Vicia Faba) as an Exciting Cause of Hay Fever and Asthma. Parlato, Salvatore J.: Riv. Sanitar. Sicil., (Palermo) **20**: 1, 1932.

The studies which led to the conclusion that asthma and hay fever were caused by the pollen of the fave bean were made during the years 1924, 1925, and 1926. Although this observation was new and original, it was withheld from our journals because it was thought that an isolated case such as this one, would not prove interesting or important to the American allergist, especially in view of the commonly accepted theory that the pollens of cultivated plants, like beans, do not cause allergic symptoms.

However, Igino Biddau in 1929 reviewed a clinical entity which has become known in the Italian literature as "favismo" and reported five cases of death which he attributed to this condition. He stated that "the symptoms of 'favismo' are manifestations like anaphylactic shock due to a contact of a hypersensitive individual with a 'quid', an unknown substance which is contained in the flowers of the fave bean." He further noted that "this substance is introduced into the individual's body through inhalation." He quoted Lotti and Ferrannini, Manai and Puxeddu, Frugoni and Lusena that in these cases, we are "dealing with an anaphylactogen which is thrown off into the air by the flower of the fave bean." As further evidence of allergy, he cited the strong hereditary tendency in which several members of the same family, including small children, manifested symptoms of hypersensitiveness.

This bean is grown extensively in southern Italy, Sicily, Sardinia, and in most of southern Europe, England and in Canada. In America, it is cultivated principally in Louisiana and California, and on a smaller scale it is found on farms and backyards in the northeast, particularly those which are owned by recent arrivals from Italy or other southern European countries.

The writer gives a full description of the structure and cultivation of this bean. The characteristics of its pollen are given in detail and illustrated by several original photomicrographs. Pollen plates showed that sufficient quantity of the pollen gets into the air so that a hypersensitive person can readily develop allergic symptoms through inhalation.

The case which is reported is that of a man who had asthma and hay fever during the late spring and early summer of each year since 1919. Clinical and immunologic tests proved that the pollen of the fave bean was the specific exciting cause. Since 1925 the patient has had complete relief by simply avoiding places where the bean was grown. This pollen is therefore identified as the "quid" or the unknown substance which Biddau thought to be the cause of "favismo."

Methods for the collection of the pollen and the preparation of protein extracts are given. Both preseasonal and seasonal treatments are outlined. It is hoped that with this new addition to our list of allergens, other cases may be accurately diagnosed and satisfactorily treated.

Results of Skin Tests on Pollen Sensitive Individuals With Protein Extracts of Different Parts of the Plant. Vallery-Radot, P., Mauric, G., Giroud, P., and Hugo, A.: Compt. Rend. Soc. de biol. **109**: 1186, 1932.

Skin tests were made upon hay fever patients with extracts made from the pollen, stamens, the plant with the exception of pollen and stamens, and the roots of the *Dactylus* plant. The intensity of the reaction at the end of ten minutes was measured in millimeters. The results, given in a table, show that nearly equal reactions are obtained by the use of pollen extract and stamen extract. The extract of the plant without pollen and stamens gave slightly weaker but still markedly positive reactions. The extract of the root, however, appeared to possess no antigenic properties.

Sensitivity to Acacia. Maytum, C. K., and Magath, T. B.: J. A. M. A. **99**: 2251, 1932.

Solution of acacia injected intravenously has been shown to be beneficial in combating hemorrhage and surgical shock. The following investigation was made of the possibility of development of sensitivity to acacia. Six normal rabbits were given 50 c.c. of solution of acacia intravenously. The dose was repeated at intervals of several days, three times. Four weeks after the last injection, the rabbits were injected with 2 c.c. of acacia intravenously. No symptoms of shock were observed. Different results were obtained with guinea pigs. Of nineteen guinea pigs injected with acacia, upon reinjection after a suitable incubation period, seven showed no anaphylactic symptoms, four showed mild symptoms, three severe symptoms, two very severe symptoms, and three died. It is concluded that under certain conditions, sensitivity to acacia may be induced. A case report is given of a patient who suffered a slight reaction after an intravenous injection of acacia. An injection of acacia had been given several months previously. The anaphylactic symptoms yielded to 0.3 c.c. of epinephrine.

The authors consider that there is no danger to the patient in the first dose of acacia if the solution is properly prepared, but that any subsequent dose given after an elapsed period of three weeks or more should be administered cautiously and the patient watched for the possibility of development of anaphylactic symptoms.

Some Remarks on the Treatment With Caffein Derivatives of Asthmatic Bronchitis in Children. Herlitz, C. W.: Acta paediat. **13**: 203, 1932.

In the treatment of acute attacks of asthma in small children, drugs such as adrenalin, atropin, urethane and chloral, while rapidly effective have certain practical disadvantages. Adrenalin and atropin must be administered by injection, and it is moreover difficult to estimate the dosage for small children. The after-effects of urethane and chloral are unpleasant for the child, and in chloral there is also an unpalatable taste. Certain purin derivatives such as caffein, theobromin and theophyllin have been suggested for their efficacy and practicability. The author undertook to find suitable doses of caffein compounds for different ages, the proper combination of these compounds, and a not unpleasant means of administration. The result of his investigation is a recommendation for a preparation, Infobronc. It is a tablet to be chewed, pleasant to the taste, and containing 0.015 gm. theobromin-calcium-salicylate and 0.035 gm. theophyllin. The effect on asthmatic attacks in children is reported to be rapid and satisfactory with a minimum of uncomfortable after-effects.

Gastric Intolerance of Hemorrhagic Form. Tzanck, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **48**: 585, 1932.

Observation of a relatively large number of operations on the stomach which revealed no apparent lesion led to the consideration that certain hemorrhagic phenomena might, like eczema, urticaria, and asthma, be manifestations of an organic hypersensitivity. A careful inquiry revealed an allergic background in these patients.

Specific Hypersensitiveness to Own Breast Milk. Duke, W. W.: J. A. M. A. **98**: 1445, 1932.

A case report is given of a woman of strong allergic family history who continued to secrete small amounts of milk seven years after the weaning of her last child. She also gave a history of prolonged eczema, caused apparently by sensitiveness to egg and to heat. Upon an egg free diet and treatment for increased tolerance to heat, she improved but was not completely relieved. It was then found that she gave a positive skin reaction of considerable severity to dilutions of her own breast milk. A passive transfer of this sensitivity was made by the Prausnitz-Küstner method. Loss of the patient's sensitiveness rapidly followed subcutane-

ous treatment with her own breast milk and soon the secretion of breast milk ceased.

Skin Reactivity of Mothers and Infants to Gonococcus Vaccines. Robak, A. J., and Greengard, J.: Proc. Soc. Exper. Biol. & Med. **30**: 117, 1932.

Skin tests with gonococcus filtrate and vaccine from diluted gonococcus broth cultures were carried out upon twenty-six adults (mothers), and one hundred and twenty infants, ranging in age from two weeks to two years. The same dosage was given to infants and adults; the injected area was measured twenty-four hours later, and the length and width of the reaction were noted. All adults studied gave large reactions, while reactions in infants were much smaller.

Similar results have been noted in reactions to staphylococcus, diphtheria and scarlet fever streptococcus antigens. The authors conclude that the phenomenon ("anergy") is due to an underdeveloped mechanism for dermal reactivity in early age.

A Nonspecific Cutaneous Sensitivity Which Is Passively Transferable to the Normal Human Skin. Walzer, M.: J. Immunol. **23**: 99, 1932.

In a preliminary report a phenomenon is described which demonstrates that certain sera, when injected into normal skins, have the power of inducing a nonspecific hypersensitiveness which cannot be differentiated from specific hypersensitiveness by a single intracutaneous test.

In the course of studying more than two hundred cases of atopic hypersensitiveness by indirect method of testing, three such sera were found; that is, the reaction in the sensitized site was greater than that obtained on a normal site with the same intracutaneous test regardless of the substance with which the injected site was subsequently tested. The result occurred even when the sites were tested with physiologic saline, distilled water or unaltered human serum. Practically all normal skins could be nonspecifically sensitized with these three sera. Therefore a Prausnitz-Küstner test cannot be considered positive unless the possibility of a nonspecific hypersensitiveness at the injected sites has been eliminated by a control test with physiologic saline on one of the sites.

Increased Suspension Stability of the Erythrocytes. Schulhof, K.: J. A. M. A. **100**: 318, 1933.

In medical literature there has been frequent mention of rapid sedimentation rates, but little attention has been given to slow sedimentation rates. It is suggested that the fact of the frequent occurrence of a slow rate may have been overlooked through an inadequate technic. In the course of a study on sedimentation rates it was observed by the author that there was a marked tendency on the part of allergic individuals towards a slow sedimentation rate. The present study is made upon

sixty-three patients who gave either an undoubted or a probable history of allergy. A Linzenmaier's tube containing 0.2 c.c. of a 2 per cent solution of sodium citrate was filled to mark 1 with about 0.8 c.c. of the patient's blood and inverted a few times. It was left standing in a rack and the time noted when the clear column of the plasma above the erythrocytes reached the successive millimeter marks (6, 12, 18, 24) on the tube. In normal health, the column of the plasma reaches the mark 18 in about ninety minutes and is somewhat faster in women.

In the present analysis, 200 minutes for mark 18 was taken as the arbitrary lowest limit of a very slow rate. In the sixty-three patients studied, fifty-three had very slow rates, three moderately slow rates, and seven normal or fast rates.

The normal or fast rates, it is suggested, may be explained by the findings of complications, especially infections, that tend to accelerate the normal rate. Thus the slow rate is masked. A reversal of this process sometimes occurs so that an allergic individual may show a slow rate in the presence of a serious infection of short duration. The interaction of the two opposite tendencies should be taken into consideration in the diagnostic and prognostic evaluation of the sedimentation rates. Postoperative accidents may occur in patients with pathologically slow rates. The very slow sedimentation rate of the erythrocytes appears to be a constant symptom in allergic individuals. A further striking feature brought out in the investigation was the frequency of slow sedimentation rates among apparently nonallergic close relatives of allergic patients.

A Study of Pannus Formation in the Cornea of Rabbits. Julianelle, L. A., and Morris, M. C.: Proc. Soc. Exper. Biol. & Med. **30**: 295, 1932.

Former studies on pannus formation in the rabbit led to the belief that the pannus might be a manifestation of bacterial hypersensitiveness. Hence it was decided to study vascularization of the cornea as an allergic response. Rabbits were sensitized to *Staphylococcus aureus*, *Bact. granulosis*, pneumococcus, diphtheroids and indifferent streptococci. The most successful method was scarification of the cornea with a scratch reaching from below the sclerocorneal margin to the pupil, followed by instillation into the conjunctival sac of two drops of a young, actively growing culture. The treatment was repeated at weekly intervals. *Staphylococcus aureus* proved to be the most effective sensitizing antigen. Following the first three or four instillations of the antigen no visible reaction took place. From the third to fifth inoculations the cornea underwent a vascularization and increasing cloudiness. With repeated inoculations the corneal vessels formed small fine loops which showed anastomoses and later descended over the cornea as a curtain of single vessels terminating in crow-foot or brushlike processes. Eventually vessels appeared from all directions reaching centripetally from the entire circumference of the cornea. As long as the instillations were continued it was possible

to keep the pannus and clouding present. Pannus could be maintained in this manner for months. With discontinuance of the instillations, the cornea cleared.

In further experiments the cornea was sensitized to purified crystalline egg albumen, by direct intracorneal injection or by combined scarification and instillation or egg albumen once a week. The corneal changes previously described were reproduced. Rabbits receiving intracorneal injections of sterile physiologic salt solution showed no increasing reactivity to successive injections. It is concluded that vascularization of the cornea of rabbits may accompany direct sensitization to live bacteria or native proteins such as egg albumen.

Observations on Lung Ventilation in Bronchial Asthma. Lewis, W. H.: Ztschr. f. d. ges. exper. Med. **82**: 71, 1932.

Observations were made during and after dyspneic attacks and include findings on reserve air, complementary air, vital capacity, respiration frequency, minute volume, inspiration and expiration time, ventilation equivalent for oxygen and carbon dioxide, and in a few instances residual air.

Eighteen asthmatic patients (ten men and eight women) were observed in attacks of dyspnea. Ages ranged for twenty-three to seventy years, the duration of asthmatic symptoms from 1¼ to 44 years. Most of them had received previous therapy of various kinds with varying results. In this investigation, the therapy employed was principally the inhalation of an adrenalin-water-glycerin spray. Spirometric observations were made upon the patients in the hospital.

It was shown that the vital capacity in asthmatic dyspnea was below the average for the normal individual. Therapeutic improvement resulted in an increase in the volume, the increase being in direct relationship to the degree of improvement. The complementary air was in most cases very greatly reduced. In 13 out of 18 cases, therapy brought about an increase. The reserve air showed a reduction from the normal of from 1500 cm. to 800 cm. and without exception was raised by therapy. The vital capacity fell in every case below the normal. Therapeutic relief from attack showed in every case an increase in vital capacity, not, however, in direct relationship to the degree of subjective improvement. The residual air was found to be above the normal average. In most cases the minute volume was below or within the normal limit.

During attacks most asthmatic patients were found to have a subnormal oxygen equivalent. This was raised by therapy. It was found that in several with the improvement of the asthmatic attack, more carbon dioxide was excreted per unit of ventilation. Respiration frequency during dyspnea was in most cases normal. The ratio of the inspiration-expiration time was found to be greater than that of the normal individual.

Graphs and very full tables are given.

Book Reviews

ASTHMA, HAY FEVER AND RELATED DISORDERS. A GUIDE FOR PATIENTS. SAMUEL D. FEINBERG, M.D., F.A.C.P. Cloth, pp. 124, illustrated, Lea and Febiger, Philadelphia.

This is the third manual published in recent years the expressed purpose of which is to acquaint patients with allergy with useful facts. Unlike its predecessors, it is expressly for the laity (although the publishers state that it should be helpful to every physician). Consequently, its simplicity of style and terms makes it easily understandable. It is a small book and contains essential facts. It is a guide for patients and, as such, is very well done.

EL ASMA Y OTRAS ENFERMEDADES ALERGICAS. C. JIMENEZ DIAZ. Paper, pp. 999, Editorial Espana, Madrid, 1932.

This is the largest treatise on allergy that has been published. It is divided into two sections: (A) a general study of mechanisms underlying allergy, and (B) clinical manifestations. The latter is again divided into two parts. The first treats particularly with asthma and elaborates upon the pathologic and clinical aspects of the disease. The second includes cutaneous and digestive allergies. The arrangement of the subject matter follows a logical sequence. A voluminous bibliography is appended, and the important literature in English, German, French and Spanish is well represented.

The author has commendably presented his subject from a broad point of view, and although his own studies are well represented, opinions of others are clearly stated. As such it is a comprehensive monograph. One cannot fail to be impressed with the immense amount of labor it must have taken to assemble a presentation of this character. This book should serve a useful purpose, particularly in Spanish-speaking countries, and be a notable addition to any medical library.

SKIN DISEASES AND NUTRITION; INCLUDING THE DERMATOSES OF CHILDREN. ERICH URBACH, M.D. Authorized English translation by Frederick Rhem Schmidt. Cloth, pp. 242, illustrated, Wilhelm Mandrich, Vienna, 1932.

This work is predicated upon the observations of investigators who maintain that the skin participates in the various metabolic changes within the body. Ionic rearrangements and chemical adjustments take place in response to absorption from the alimentary tract. As a consequence, treatment of many dermatoses is directed at the gastrointestinal canal.

Diets are given in detail for various conditions, and elaborate devices for intestinal lavage are pictured.

A considerable portion of the book is devoted to allergic skin disorders. The usual diagnostic methods and elimination diets are discussed. The author then gives his propeptan treatment in considerable detail.

There is an excellent bibliography and also a supplement with food charts and tables well worked out. The book contains a good deal of interesting information, but its point of view is frequently too individualistic to be accepted whole-heartedly.

Correspondence

San Francisco, Calif.
February 9, 1933.

The Editor,
Journal of Allergy.

Dear Sir:

I noticed recently, in making a review of allergy literature for the Journal of Pediatrics, that following Doctor Bain's and my report on the study of the allergic skin test antibody, Doctor Sherrer published a study precisely similar, and with the same conclusions, without any mention of our previous report. Our article appeared in THE JOURNAL OF ALLERGY on page 177 of volume II, March, 1931, and his is on page 467, appearing some months later. It seems to me only fair that some priority on this study should be established.

Sincerely yours,
(Signed) Francis Scott Smyth, M.D.

Errata

"Urinary Porteoses in Bronchial Asthma—A Clinical Study," January, 1933, p. 137, line 26, "10 c.c. of ether" should read "100 c.c. of ether"; and on line 35 "1:100 solution" should read "1:1000 solution."

"Intolerance to Whitfield's Ointment as a Cause of Failure in the Treatment of Epidermophytosis," January, 1933, p. 146, "Sabourraud" throughout should read "Sabouraud."